Self-Reported Respiratory Health Effects Following CS Riot Control Agent Exposure in Army Officer Trainees

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DEDICATION

This thesis is dedicated to my beautiful and talented wife Cynthia. We have been through both enjoyable and trying times over the past ten years, I am thankful to have been through it together.

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Matthew J. Holuta

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ABSTRACT

Self-Reported Respiratory Health Effects Following CS Riot Control Agent Exposure in Army Officer Trainees

Captain Matthew J. Holuta, Master of Science in Public Health, 2016

Thesis directed by: MAJ Joseph J. Hout, PhD, Department of Preventive Medicine and Biometrics

The riot control agent (RCA) *o*-chlorobenzylidene malononitrile (CS) is used to facilitate a realistic training environment as part of a military training task known as mask confidence training (MCT) in which soldiers enter an enclosed structure containing a concentration of CS, perform a variety of tasks, and ultimately remove masks prior to exiting the chamber. The CS causes immediate but transient ocular, respiratory, and dermal irritation. This research prospectively studied the association between post-MCT symptoms of self-reported acute respiratory illness and CS exposure among a cohort of 74 officer trainees enrolled in a U.S. Army Basic Officer Leadership Course (BOLC) held June 12th through July 25th, 2015. Developing new-onset symptoms of acute respiratory illness during the week following MCT was dependent on exposure levels above 1.5 times the Immediately Dangerous to Life and Health (IDLH) concentration (3.00 mg/m^3) which was also associated with three excess cases of acute respiratory illness symptoms per 25 participants compared with exposure below 3.00 mg/m^3. An

increase of 1.00 mg/m^3 in individual CS exposure concentration was associated with 5.6 times greater odds (95%CI 1.3-36.9) of developing symptoms of acute respiratory illness one-week after MCT. Those with a history of respiratory allergies developed acute respiratory illness symptoms with exposure to lower CS concentrations than those without respiratory allergies. The study lacked the statistical power to create a multivariate model or to analyze stratum specific effects. CS exposure exceeding IDLH may lead to excess risk of acute respiratory illness, and the presence of a threshold effect at 1.5 times IDLH is plausible.

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CHAPTER 1: INTRODUCTION

INTRODUCTION

The riot control agent (RCA) *o*-chlorobenzylidene malononitrile (CS), commonly known as CS or tear gas is known for its debilitating ocular, respiratory, and dermal irritant effects (36; 43). U.S. Army soldiers are exposed to CS during a common military training task known as mask confidence training (MCT), where CS is thermally disbursed as a training aid to build confidence in a soldier's military protective mask (17). Previous studies by Hout et al. described an association between CS exposure above occupational exposure limits (OELs) during MCT and an increased rate of acute respiratory illness in basic trainees (28). Furthermore, Hout's studies demonstrated a dose-response relationship between CS concentration and rate of acute respiratory illness, and provided evidence of a temporal relationship between CS exposure and acute respiratory illness in a military training population (27; 28).

The aim of this research was to further evaluate the association between CS exposure above OELs during MCT and acute respiratory illness in a different training population. The study used a prospective observational cohort design to examine the incidence of self-reported new-onset respiratory outcomes during a one-week follow-up period in U.S. Army Officers enrolled in an Army Medical Department (AMEDD) Basic Officer Leadership Course (BOLC). Self-administered questionnaires were used to assess respiratory symptom severity, demographic information, and other variables of interest including respiratory allergies, asthma, smoking, fitness level, previous exposure to CS, and self-reported contact with potentially infectious individuals. Personal breathing zone sampling was used to assess CS exposure concentrations. Respiratory outcomes and symptoms of acute respiratory illness in the study population were

evaluated for dependence on exposure above or below several OEL derived threshold concentrations based on the Immediately Dangerous to Life and Health (IDLH) value of CS. The distribution of individual CS exposure concentrations were evaluated for association with respiratory outcomes in the population. Thus, the study builds upon previous evidence by evaluating the association between self-reported symptoms suggestive of acute respiratory illness and individually quantified CS exposure levels while accounting for potential risk factors in a military training population.

BACKGROUND AND LITERATURE REVIEW

The purpose of this review was to outline what is known about CS exposure and related respiratory health effects in military training populations, and to identify a method to quantify respiratory symptom severity through self-report. It provides an overview of MCT and serves to identify covariates in the population that could confound or modify the relationship between CS and acute respiratory illness. The characteristics, uses, and health effects of CS are summarized along with a review of acute respiratory illness and related symptoms in military training populations and the association between acute respiratory illness and CS exposure during training are included.

Basic Officer Leadership Course (BOLC)

This study prospectively observed a cohort of AMEDD officers completing initial entry training called the BOLC. Individuals commissioned to serve in the various AMEDD corps include physicians, nurses, dentists, veterinarians, and various administrative and technical specialties. Due to the strict medical screening criteria an individual must meet to enter military service, the BOLC population was expected to be free of chronic respiratory disease, physical disability, and was healthy and fit in

comparison with the general U.S. population (15). The BOLC for AMEDD officers is offered several times each year with one iteration, which was followed in this study, specifically tailored toward physicians, medical students, dentists, and veterinarians.

The purpose of BOLC is to prepare new officers to work in the AMEDD, it focuses on leadership, basic soldiering, and tactical medical skills (51). The course is completed in six weeks with the second half held in a field training environment. Examples of training include mission planning, land navigation, basic marksmanship, and chemical, biological, radiological, and nuclear (CBRN) training. One component of CBRN training is protective mask confidence training, which occurs on one of three days during the second week of the field training phase (51).

The studies by Hout et al. evaluated the relationship between CS exposure and acute respiratory illness in a Basic Combat Training (BCT) population, which is the initial entry training for those enlisting in the U.S. Army (27; 28). Although BOLC and BCT populations conduct many of the same training tasks including MCT, BOLC trainees have less exposure to close living conditions, and are in a less physically and psychologically stressful environment. Additionally, the training environment in BOLC is different compared to that of BCT since basic trainees have minimal free time and share living quarters, which are often a large open bay room (55). Unlike BCT, BOLC trainees are off-duty during the nights and weekends, and live in single occupancy quarters except during the field training exercise (51).

CS Characteristics and Use

Characteristics

In the late 1950s, the U.S. Army began using CS as its designated riot control agent (RCA) (50). Two chemists, Ben Corson and Roger Stoughton, developed CS (commonly known as tear gas) in 1928; the abbreviation CS is derived from the first letter of their last names (43). CS has a melting point of 93°C, and can be aerosolized when heated. The U.S. Army aerosolizes CS by both thermal canister and by heating capsules containing CS (18; 36). Disbursed CS quickly causes a burning sensation on unprotected surfaces of the body and nearly instantaneous irritation of the eyes, respiratory system, and skin (36). CS is used as a RCA because of its low toxicity and immediate but transient incapacitating sensory irritation. In a riot-control situation, CS is deployed via thermal canister, and although used in other military training situations, CS canisters are not used in mask confidence training (17).

Mask Confidence Training

MCT is an individual military training task used to verify the function and build confidence in a soldier's protective mask (17). The military protective mask is a full-face respirator with a cartridge capable of filtering many chemical and biological agents (19). U.S. Army training regulations require MCT using CS for field units on an annual basis and before deployments, and Army recruits complete MCT during BCT (17). MCT is generally conducted inside a designated enclosed building or "chamber" in a military training area. A concentration of CS is generated during MCT by heating CS capsules either with a hot plate or by placing them on top of an upside down tin can that is heated with a Sterno® can (14; 18). A chamber operator generates a concentration of CS using a

standardized protocol prior to the start of the MCT event by heating the indicated number of CS capsules (chamber volume (m^3) x 0.0107); to maintain the concentration, one capsule is added per 50 trainees exiting the chamber (52).

The irritant properties of CS facilitate a realistic training environment to build confidence in a soldier's protective equipment. Soldiers don protective masks prior to entering the chamber, and once inside the chamber they are guided through a number of exercises designed to verify the fit of the mask and to increase their respiration rate. The disbursed CS will reveal if an individual's protective mask is properly fitted and functioning by causing ocular and respiratory effects and a burning sensation on exposed skin. After completing the required exercises and prior to exiting the chamber, soldiers remove the mask and take an unprotected breath. Immediate but transient ocular and respiratory irritation is experienced which serves to reinforce the importance of proper maintenance and fit of the protective mask.

Health Effects

Routes of CS exposure include inhalation, dermal and ocular contact, and ingestion if mucous is swallowed during exposure. The eyes and respiratory system are predominantly affected by CS due to irritation of the associated mucous membranes and concomitant inflammation and pain (36). Consequently, CS causes significant, often incapacitating, ocular and respiratory irritation within thirty seconds of exposure (36; 43). The incapacitating symptoms that follow exposure include "intense burning of the eyes, profuse lacrimation, blepharospasm, burning sensation of the nose and respiratory tract, excessive salivation, tightness in the chest and a feeling of suffocation" (36). It also causes a burning sensation on exposed skin which intensifies at higher ambient

temperatures, and when the skin is wet (43). The acute symptoms of exposure persist for a short time after exposure has ended, in most cases full recovery is expected within approximately 30 minutes (56).

A number of studies have noted that exposure to CS, especially at high concentrations, resulted in adverse respiratory health effects well beyond the cessation of exposure (2; 20; 36; 40; 43; 50). Pipkin first noted a possible relationship between CS exposure during military training and acute respiratory illness, and a case study by Thomas et al. noted acute pulmonary effects leading to hospitalization of military personal in a situation where CS exposure was followed by strenuous physical activities (40; 50). The irritant effects are related to concentration and duration of exposure, and there is evidence that low concentrations even over a longer period are less hazardous than shorter high concentration exposure (43). A protracted or highly concentrated exposure may increase an individual's susceptibility to adverse health effects such as coughing, reduced respiratory function, runny nose, or headache in the 12 to 24 hours after exposure (20; 31; 43). A study of individuals previously exposed to CS by Arbak et al. found repeated high intensity exposure may reduce lung function, and was associated with adverse effects on the respiratory system observed months and years after exposure (2). Moreover, CS exposure has the possibility of aggravating pre-existing respiratory conditions such as asthma, which can increase susceptibility to a severe exposure response (43; 56). The documented health effects related to CS exposure support the plausibility that it could increase susceptibility to acute respiratory illness or lead to other adverse health effects.

Exposure Guidelines

Occupational exposure guidelines for CS have been published by multiple agencies because of its dose and time dependent health effects. The Occupational Safety and Health Administration (OSHA) promulgated a Permissible Exposure Limit (PEL) of 0.40 mg/m^3, which is an 8-hour time weighted average that must not be exceeded during a normal work day (37). The American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Value - Ceiling (TLV-C) is 0.39 mg/m^3 which is a concentration that should not be exceeded at any time in an occupational environment (1). It also includes a skin notation indicating that skin, eye, and mucous membrane exposure are contributors to overall exposure (1). The Immediately Dangerous to Life and Health (IDLH) value published by the National Institute of Occupational Safety and Health (NIOSH) is 2.00 mg/m^3 (34). The purpose of an IDLH value is to identify a concentration at which a worker could escape from a contaminated environment in the event of a respirator failure without immediate or long-term permanent health effects (34). Eye and respiratory effects that could result from up to 30 minutes of exposure, which could prevent escape from an area in the event of a respirator failure are also considered in determining the IDLH value. The TLV-C and IDLH values are important OELs to consider for the short duration exposure experienced in MCT, and also of note, the threshold for eye irritation is 0.004 mg/m^3 (43).

Acute Respiratory Illness

Overview

Acute respiratory illnesses are common globally, and represent a significant cause of morbidity in the U.S. military leading to lost productivity (24; 54). They characterize

a group of illnesses that can affect the upper and lower respiratory system and may include an associated fever. A variety of terms, including acute respiratory illness, are used to describe the various respiratory infections whose accompanying symptoms tend to be non-specific and include "nonfebrile common cold with congestion; febrile illness with malaise, sore throat, and cough" (41). Even in less severe cases, the resulting degradation of work performance or lost productivity from symptoms is significant. Accordingly, morbidity associated with symptoms is an important indication of the impact of the illness regardless of cause (26).

Military Populations

Important pathogens associated with acute respiratory illness in military populations include group A streptococcus, adenovirus, influenza A, pneumococcus, rhinovirus, bordetella pertussis, mycoplasma and chlamydophila pneumonia, respiratory syncytial virus (RSV) and coronaviruses (41). Incubation periods vary between pathogens with those likely to occur during the summer ranging from one to three days (41). The symptoms of the common cold tend to peak at two to three days after infection (26). Compared with the U.S. general population, military recruits are at greater risk for acute respiratory illness due to a number of unique risk factors associated with military service, particularly the influences of living in close quarters and working in stressful environments (3; 24; 39; 47). The symptoms associated with acute respiratory illness can negatively impact a service member's functional status even in cases when care is not sought (42; 47).

Risk Factors

Military recruits are at particularly high risk for acute respiratory illness during their basic (initial entry) training, where individuals from around the country train in a physically and psychologically stressful environment (23; 39; 55). Recruits come from varied backgrounds and locations and, as a result, are likely exposed to pathogens for which they lack immunity when they are brought together for initial training. Recruits also live in close living and working conditions which can contribute to the transmission of respiratory illnesses, especially in the first few weeks of training (7; 41). Similarly in the non-recruit military population, respiratory disease tends to develop more frequently several weeks after arrival at a new duty station when compared with a year after arrival (7). Soldiers completing BCT or BOLC are new recruits with the risk factors shown to increase susceptibility for acute respiratory illness as in other recruit populations, however, BOLC trainees have less exposure to the risk factors when compared with basic trainees.

Additional factors thought to affect susceptibility to respiratory illness in the general population include: smoking, respiratory allergies, asthma, sleep deprivation, fitness level, physical stress, and psychological stress along with close contact with infectious individuals (8-12; 53; 54). In multiple studies of risk factors for acute respiratory illness, Cohen et al. identifed that reporting less than seven hours of sleep per night, smoking cigarettees, and chronic long-term stress are risk factors that may increase susceptibility to the common cold (9-11). Physcological stress and heavy physical activity are thought to increase suceptibiltiy to acute respiratory illness while moderate physical activity may be protective (26). In addition, conditions or habits which affect the respiratory system such as asthma, respiratory allergies, and smoking may increase an

individual's risk of acute respiratory illness (39). Finally, exposure to potentially infectious individuals was found as an independent risk factor in a case-control study of respiratory tract infection risk factors by van Gageldonk et al. (53).

CS Exposure and Acute Respiratory Illness

There is evidence of a dose-response relationship between adverse respiratory health effects and exposure to CS in training and riot control situations (2; 20; 43; 50). Furthermore, several studies found an increased rate of acute respiratory illness based on applicable International Classification of Diseases Version 9 (ICD-9) coded diagnoses in training populations exposed to CS during MCT (27; 28). While in the chamber during MCT, the irritant properties of CS are immediately evident on exposed skin, and on the eyes and respiratory tract once the protective mask is removed. What is less evident is whether there are any long-term respiratory effects that manifest in chronic or persistent symptoms or that influence the occurrence or worsening of existing respiratory conditions, such as asthma or respiratory allergies.

Previous research of MCT related CS exposure by Hout et al. noted that soldiers in BCT were exposed to CS concentrations greater than OELs during MCT and had an increased rate of clinically diagnosed acute respiratory illness in the week following MCT (28). In response, the Army issued a directive reducing the prescribed number of capsules used during MCT in an effort to decrease CS concentrations during training (52). In a follow-up study by Hout et al., CS concentrations continued to vary substantially during the course of MCT events, and while there was an overall reduction, concentrations above the ACGIH TLV-C were still observed (28). Furthermore, the rate of acute respiratory illness continued to be greater in the week after MCT when compared

to the rate in the week prior to MCT, a finding that was independent of previously identified risk factors in the BCT population such as building type and training week (28; 55). Additionally, the rate of acute respiratory illness was significantly greater when CS concentrations exceeded the ACGIH TLV-C (27; 28). Neither study by Hout et al. was able to evaluate other important risk factors for acute respiratory illness in the BCT study population, nor was personal exposure sampling feasible due to the training environment. However, these studies provide evidence of a temporal, as well as dose-response relationship between CS exposure and acute respiratory illness in a military training population.

Self-Report Methods for Respiratory Illness Identification

Underreporting in Military Populations

Military service members may encounter a number of barriers discouraging them from seeking care for an acute respiratory illness including the amount of time it may take to be seen by a healthcare provider. In a study of infectious disease in deployed service members by Soltis et al., a survey was used to investigate the frequency of self-reported acute respiratory illness, seeking care for that illness, and degradation of work performance related to that illness (47). Of the 37% self-reporting an acute respiratory illness, 33% reported degraded job performance, and 18% sought medical care (47). In a similar cross-sectional study of military service members, Sanders et al. found that 69% self-reported an acute respiratory illness of which 17% sought medical care (42). In order to receive medical care, a trainee must pass through several levels of health screening prior to an appointment with a healthcare provider. This process is often time-consuming and can lead to absence from required training events. As a result, it is

possible that not all who are symptomatic seek care because missed training requirements may delay graduation or result in the need to repeat portions of training (39). Despite not seeking medical attention, an individual may have reduced functional status due to respiratory illness that could impair performance (39; 47). Thus, clinically diagnosed cases such as those assessed in the study by Hout et al. may not represent the full extent of acute respiratory illness in a military population.

The Jackson Method

Many studies of acute respiratory illnesses have used the self-report of symptom severity to determine the beginning, presence, and duration of illness (5; 25; 49). Since the 1950s, the criteria-based method of case identification developed by Jackson et al. has been the "best validated and most widely used" tool for assessing self-reported respiratory symptoms suggestive of acute respiratory illnesses (30; 49). In the Jackson Method, eight symptoms (sneezing, rhinorrhea, nasal obstruction, sore/scratchy throat, cough, headache, malaise, and chills) are rated on a scale from absent to severe (0= absent, 1= mild, 2= moderate, 3= severe) by a study participant (49). Symptom severity scores are measured prior to exposure and again following the exposure. The net score is determined by subtracting each symptom's follow-up score from that symptom's baseline score. The net symptom severity score is summed and cut points are used to designate an acute respiratory illness in those also self-reporting a cold (30). The original cut point was a Jackson score greater than 13, but was later modified to a symptom score cutoff of greater than five, which has been used extensively to identify cases in studies of rhinovirus (30; 49).

Zitter et al. used the Jackson Method in a natural experiment to assess symptoms suggestive of acute respiratory illness in airline passengers. The aim was to assess the impact of recently implemented air recirculation systems in commercial airliners on respiratory health (57). Volunteers were grouped by aircraft type to allow a comparison of outcomes between aircraft with air recirculation systems and those that did not recirculate air (57). A questionnaire, which included the Jackson Method, was employed to determine a participant's baseline symptom score. Other covariates thought to be important were also documented at baseline and individuals who thought they might already have a cold were excluded. Post-flight symptoms were assessed with a questionnaire in a follow-up period of five to seven days and the net Jackson Method scores were used to identify cases (57). The odds of symptoms meeting case criteria between the two types of air circulation systems in airliners did not differ significantly. The study employed the Jackson method to quantify and compare self-reported respiratory illness symptoms meeting case criteria between two groups with different exposures.

PUBLIC HEALTH AND MILITARY SIGNIFICANCE

Military populations, especially new recruits, are at risk for acute respiratory illness, and CS has been shown to affect respiratory health beyond the expected recovery period. Past research assessed the effects of CS exposure at varying concentrations on clinically diagnosed acute respiratory illness, but has not quantified unreported symptoms or associated risk factors potentially affecting outcomes over a follow-up period after MCT. Furthermore, the previously observed relationship between CS and respiratory outcomes has not been evaluated in the BOLC population or with individual exposure

data. Self-reporting methods may provide a more comprehensive measure of the impact of exposure due to underreporting in military populations. Therefore, utilizing self-reports to document symptom severity and important risk factors in the study population before and after CS exposure may provide additional information about post-MCT respiratory health effects. Since MCT training occurs in the BOLC, there is an opportunity to evaluate the association between CS exposure and respiratory outcomes in a unique group with potentially different risk factors compared to a BCT population. Documenting individual exposure and self-reported health outcomes could further clarify the potential health effects in at-risk populations and results from this study could influence policy regarding training to reduce respiratory morbidity and lost duty days.

CHAPTER 2: METHODS

RESEARCH GOALS

The purpose of this research was to compare the incidence of self-reported respiratory outcomes following CS exposure during MCT between groups exposed above and below CS threshold concentrations including and derived from the IDLH value, during the week following MCT. The temporal relationship between CS exposure and acute respiratory illness symptoms was evaluated in a one-week follow-up period by quantifying individual CS exposure and documenting baseline and post-MCT self-reported respiratory symptom severity among a cohort of AMEDD BOLC trainees.

Hypotheses

This research tested the following hypotheses:

1. Respiratory outcomes meeting case criteria will be associated with exposure above the IDLH concentration for CS.
2. Respiratory outcomes will increase as CS exposure concentration increases.
3. Attributes of the study population will influence the observed relationship between CS exposure and respiratory outcomes meeting case criteria.

Research Objectives

The primary aim of evaluating the relationship between groups exposed to CS above and below a threshold concentration during MCT and self-reported symptoms consistent with acute respiratory illness was attained through the following objectives:

1. Develop a questionnaire that includes a validated self-reporting medical surveillance tool for capturing respiratory outcomes while documenting

factors that could potentially effect respiratory outcomes including demographic information.

2. Assess individual CS exposure during the MCT event through personal breathing zone sampling.
3. Use an observational cohort study design to document baseline (pre-MCT) and follow-up (post-MCT) self-reported respiratory outcomes and other attributes of the population using the study questionnaire.

Specific Aims

The hypotheses were tested using the following specific aims:

1. Evaluate the strength of association between the distribution of individual CS exposure concentrations and new-onset self-reported respiratory outcomes meeting case criteria.
2. Evaluate the association between CS threshold based exposure groups and new-onset self-reported respiratory outcomes meeting case criteria.
3. Evaluate the association between the distribution of individual CS exposures and self-reported respiratory symptom severity scores.
4. Investigate the association between new-onset self-reported respiratory outcomes meeting case criteria and study population covariates.

STUDY OVERVIEW

This prospective observational cohort study measured self-reported respiratory symptom severity in officer trainees prior to and during the week after CS exposure. Three distinct questionnaires were developed and used to document self-reported health status and new-onset respiratory symptom severity during the study period (Appendix A).

Participants completed the baseline questionnaire, which also documented self-reported demographic characteristics and risk factors prior to MCT, and two post-exposure questionnaires given 24 hours and one-week following MCT respectively. Respiratory outcomes were identified using case criteria based on reported symptom severity scores, and personal breathing zone sampling quantified CS exposure concentrations during MCT. These data were used to evaluate the association between symptoms of acute respiratory illness and CS exposure in the population.

STUDY POPULATION

The study population included trainees enrolled in the AMEDD BOLC class held between June 12th and July 25th, 2015. The class was composed of 486 officers enrolled in the Health Professions Scholarship Program (HPSP) who were in the process of completing their education at various universities, and 60 officers who would begin medical school at the Uniformed Services University (USUHS) upon completion of BOLC. The 546 trainees enrolled in the class were divided evenly into six platoons of approximately 90 personnel. MCT took place in the fifth week of the course over three days (14-16 July) with two platoons completing the training each day.

In each of the three weeks of the field training phase of the course, trainees arrived at the field training site on Monday, remained through the week, and departed on Friday afternoon. Training was scheduled from 0600 hours to 1700 hours each day. While at the field training site, trainees slept in military tents shared by 10 to 20 individuals from the same platoon. The tents were equipped with heating, ventilation, and air conditioning systems (HVAC) which circulated filtered, fresh, climate controlled

air. HVAC systems were used to cool the tents in the evenings and at night and turned off during the working day.

Participants were recruited at the field training site prior to completing MCT. Volunteers were provided with written and verbal information about the study including the study purpose, risks and benefits of participation, alternatives to participating, the right to withdraw, and how to receive additional information. Consent was documented with signed forms and obtained prior to a subject's enrollment and participation in the study (Appendix D).

Human Subjects Research Protection

The study protocol received USUHS Institutional Review Board authorization as minimal risk human subjects research (Appendix C). Protections employed in the study included informed consent prior to enrollment, maintaining confidentiality throughout the study, securing personally identifiable information, and not altering the MCT process. All BOLC trainees were required to complete MCT as part of the BOLC curriculum and irrespective of the study. The study did not alter standard operating procedures, personal protective equipment, training tasks, or elapsed time in the CS chamber. The training staff operated and directed the MCT event in its entirety, and emergency medical technicians were present while training was in progress. Confidentiality was maintained throughout the study by assigning a unique study identifier to each participant at enrollment in order to link questionnaire and exposure data. As a result, the questionnaires did not collect personally identifiable information (Appendix A). The investigator maintained a key file linking study identifiers with each participant's name to

assign exposure and questionnaire data. The file was secured while not in use and destroyed after data were linked in the study dataset.

RESPIRATORY OUTCOME ASSESSMENT

Overview

The primary outcome of interest was respiratory symptom severity meeting criteria of the Jackson Method. Participants completed the baseline questionnaire prior to MCT and symptom severity in relation to CS exposure during MCT was assessed with the follow-up questionnaires at 24 hours post-MCT and at one-week post-MCT. Self-reported symptoms were measured and cases were identified using the rated severity of the eight symptoms indicated in the method developed by Jackson et al (30).

Enrollment and Completion of Questionnaires

The enrollment of volunteers and administration of questionnaires was synchronized with the field training exercise timeline (Appendix E). The informational briefing and recruiting occurred after trainees arrived at the field training site on the first day (13 July) of the week in which MCT occurred. Due to training schedule constraints, enrollment continued through the third training day of the week (15 July). Volunteers were provided with the study background information, gave written consent, and completed the pre-exposure survey prior to participating in the MCT event. Each individual was assigned a unique study identifier upon completing the consent form and pre-exposure questionnaire. A master key was generated during the enrollment process to match participant's name and respective study identifier and to allow exposure data and follow-up surveys to be linked accurately. Approximately 24 hours after MCT, participants completed the first post-exposure questionnaire at the field training site. The

final post-exposure questionnaire was also administered at the field training site approximately one week (five to seven days) after completing MCT.

STUDY QUESTIONNAIRE

The three distinct self-administered questionnaires were used to document self-reported respiratory symptom severity and study population attributes in a temporal sequence to identify new-onset respiratory outcomes 24 hours and one week after CS exposure (Appendix A). Previously validated constructs were used in the questionnaire where possible and all questionnaires used the Jackson Method to measure respiratory symptom severity and determine case status. Items assessing potential risk factors were incorporated into the questionnaire to account for possible confounding or modification of the relationship between CS exposure and new-onset cases. Self-reported demographic characteristics documented in the study questionnaire included: age, gender, rank, height, weight, and assigned unit. To identify adverse health effects after exposure, information was collected about conditions that could be exacerbated by CS exposure or increase susceptibility to adverse health effects including smoking history, fitness, previous exposure to CS, recent contact with infectious individuals, and history of asthma and respiratory allergies. It was also necessary to identify indications of other adverse effects potentially associated with CS exposure including degraded ability to perform vigorous physical activity and the persistence of acute exposure symptoms beyond the expected recovery period.

Baseline and new-onset symptoms were assessed using recall periods specific to each questionnaire including the three days prior to MCT, in the 24 hours since completing MCT, and in the week since completing MCT. This allowed the

measurement of symptoms and attributes preceding exposure to establish a baseline and after exposure to identify new-onset symptoms, variation in symptom severity, and any change in the selected covariates. The questionnaire was administered in paper-based format along with the study information sheet and the consent form.

The questionnaire was reviewed by a survey expert and underwent cognitive pre-testing prior to being finalized and reproduced for the study. Cognitive pre-testing was utilized to reduce reporting error by determining if a similar population interpreted items as planned by seeking feedback related to comprehensibility of questions and response anchors. Five individuals reviewed the questionnaire as part of the cognitive pre-testing, each had completed MCT in the past including two that had completed the AMEDD BOLC.

Respiratory Outcome Measurement Tool

The diagnostic tool for identification of self-reported symptoms suggestive of acute respiratory illness developed by Jackson et al. was used to document the primary outcome of interest in the study (30). The method requires an individual to report symptom severity on a scale from one (mild symptoms) to three (severe symptoms) as presented in Figure 1. The case definition used in the study was a summed net symptom score of greater than five and the self-report of a cold (25). New-onset cases were identified by subtracting baseline scores from follow-up scores (25). For example, if severity of the runny nose symptom was reported at baseline as a one, and at one-week after MCT runny nose severity was reported as a three, the net runny nose score is two. This process is repeated for each symptom and the net scores are added together to reach the net symptom severity score, which when greater than the cutoff indicates a case if the

individual also reports having a cold in the same period. Respiratory outcomes meeting case criteria indicate the presence of symptoms suggestive of acute respiratory illness.

Symptoms	Severity
Sneezing	Mild Symptoms = 1 Moderate Symptoms = 2 Severe Symptoms = 3 No Symptoms = 0
Runny Nose	
Stuffy Nose	
Sore Throat	
Cough	
Headache	
Feeling Tired	
Chills	

Figure 1. Jackson Method Symptoms and Response Anchors.

Pre-MCT Questionnaire

The pre-exposure questionnaire was used to establish the baseline of self-reported respiratory symptom severity in the three days prior to MCT using the Jackson Method. The recall period accounted for likely respiratory diseases that have short incubation periods, and allowed pre-existing cases to be identified in the study population. The pre-exposure questionnaire was also used to document demographic information and items related to relevant medical history, current health, and past CS exposure.

The self-reported demographic information was used to characterize the study population. Participants were asked to provide age, gender, rank, AMEDD corps, and training unit. Training unit was used to identify participants during the MCT event and for completion of the follow-up questionnaires. The other questions were used to describe the study population and potential trends in participants with new-onset respiratory outcomes.

Self-reported history of asthma and respiratory allergies were assessed using questions adapted from the 2014 National Health Interview Survey (NHIS) Questionnaire

(21). Fitness was evaluated with Body Mass Index (BMI) and Army Physical Fitness Test (APFT) score. Self-reported height and weight were used to calculate an individual's BMI (weight (lb.) / (height (in.)) 2 x 703) (33). Most recent self-reported APFT score was documented with a selection of three ranges: less than 180 (failing), 180 – 269, and 270 or greater. The scales used to calculate APFT scores are adjusted for sex and age, and the scores are calculated by adding the points an individual receives in each of three events: pushups, sit-ups, and a two mile run (16).

Current smoking status and smoking history were each assessed with a question adapted from the 2014 NHIS Questionnaire (22). Three questions addressed possible interaction with potentially infectious individuals; participants were asked to report if a roommate, platoon-mate, or tent-mate had a cold, cough, fever, or runny nose in the preceding week. One item addressed whether an individual had less than seven hours of sleep per night on average in the two preceding weeks, and past CS exposure (never, once, or multiple times) during MCT was assessed with one question. To identify possible care-seeking behavior, participants were asked to report how many days of work or school were missed in the previous year due to a respiratory illness.

The pre-exposure questionnaire addressed several items that were reassessed in the follow-up questionnaires using the same constructs. As applicable, questions were used to assess perceived severity of asthma symptoms and respiratory allergy symptoms using a five-point Likert scale (very mild – very severe), and two items addressed whether medications had been used to ease symptoms of asthma or respiratory allergies.

24-hour Post-MCT Questionnaire

The second questionnaire was administered approximately 24 hours after a participant completed MCT to reassess respiratory symptom severity, and to ascertain the presence of acute CS exposure symptoms as well as any change in asthma and respiratory allergy symptoms. The Jackson Method was used to document respiratory symptom severity in the 24 hour period after going through the CS chamber excluding the first hour. The recall period captured symptom severity after participants would be expected to recover from the acute irritant effects of CS.

The 24-hour follow-up questionnaire included several constructs specific to the participants' experience during and immediately after MCT. Participants were asked to report how many breaths were taken after removing the protective mask, and to rate their discomfort while in the chamber using a five-point Likert scale (very mild – very severe). One item assessed the duration of acute exposure symptoms upon exiting the CS chamber (less than 30 minutes – greater than one hour) to determine if an exceptional exposure occurred.

In the questionnaires used at each point of follow-up, three questions were used to assess symptoms of irritation and capacity for physical activity within the respective recall period. Symptoms of acute irritation were rated with a five-point Likert scale (very mild – very severe) and included: tightness of the chest, shortness of breath, feeling of suffocation, and wheezing. Another question asked participants to indicate if they had experienced symptoms related to CS exposure including: skin irritation, burning sensation or rash on the head, neck, or hands in addition to upset stomach, nausea, vomiting, or diarrhea. Participants were asked to rate change in capacity for vigorous physical activity in the follow-up period on a five-point Likert scale (much worse – much

better) using a question adapted from the 2008 Department of Defense Survey of Health Related Behaviors Among Active Duty Military Personnel (6).

One-Week Post-MCT Questionnaire

The questionnaire used for follow-up one week post-MCT used the content and structure from the 24-hour post-MCT questionnaire but omitted the items referencing the in-chamber experience and duration of acute irritant effects. The Jackson Method was used to document new-onset self-reported respiratory symptom severity in the week following CS exposure with a recall period of the week after going through the CS chamber, but excluding the first 24 hours after the event. The follow-up period allowed time for respiratory outcomes to develop in the study population. One additional question addressed adverse health effects in which the participant was asked to indicate if they had been awakened from sleep by their own coughing since CS exposure.

CS Exposure Assessment

Method

The exposure of interest was the concentration of individual CS exposure sampled while a study participant was inside the CS chamber completing MCT. CS was collected through personal breathing zone sampling using the OSHA modified NIOSH Physical and Chemical Analytical Method (P&CAM) 304 (38). Two types of sampling media are indicated when using NIOSH P&CAM 304 since thermally dispersed CS can form both a vapor and an aerosol (35). The OSHA modified NIOSH P&CAM 304 method replaces the separate polytetrafluoroethylene (PTFE) filter and Tenax TA sorbent tube with a single OSHA Versatile Sampler (OVS) in the sampling train (35; 38). The OVS contains a glass fiber filter and two sections of Tenax TA (70/140mg) sorbent that enables

collection of both aerosols and vapors (Figure 3) (45). The OVS media were pre-labeled with sequential alphanumeric codes for identification during sampling and analysis.

The sampling train consisted of an OVS sampler connected with a one meter length of Tygon tubing to either AirChek XR5000 or Universal 44XR air sampling pumps, both manufactured by SKC, Inc. (Figure 3) (44; 46). Following OSHA modified NIOSH P&CAM 304, the pump flowrate was set to 1.5 liters per minute (L/min) and calibrated with BIOS DryCal calibrators (32; 38). Sampling pumps were calibrated prior to the event and after the sampling train had been removed from an individual exiting the CS chamber. When the difference between pre and post calibration was less than five percent, the average of the two flow rates was used to calculate volume sampled (4). When the difference between pre and post-sampling calibration flow rate was greater than five percent, the samples were excluded from the analysis. Sampling pumps were started within 30 seconds of a participant entering the MCT chamber and stopped shortly after exiting. Elapsed participant time in the MCT chamber and detected CS mass were used to calculate the CS exposure concentration to avoid diluting results with unexposed sampling time.

Analysis was conducted by the U.S. Navy Comprehensive Industrial Hygiene Lab (CIHL) – Norfolk following a modification of the NIOSH P&CAM 304 protocol. The media was desorbed with toluene and analyzed using a gas chromatograph coupled to an electron capture detector (GC-ECD) (13). The CIHL lab validated the method prior to analysis obtaining a limit of quantification of 0.055 micrograms (μg).

MCT Process Description

The MCT chamber was 15 feet (ft.) by 10 ft. by 11 ft., constructed of concrete masonry unit block, and had single doors on opposite sides of the chamber (Appendix B). While the event was in progress CS was disbursed from the middle of the chamber and doors were opened when personnel entered or exited the structure. The doors were left open for approximately one hour after training ended each day to allow the CS to clear from the structure. An overview of the MCT chamber is provided in Figure 2.

On the day of MCT, the BOLC trainees were transported to the training site where they were gathered in an area used for didactic instruction located approximately 100 meters north of the MCT chamber facility. Study participants were identified from the two platoons going through the MCT chamber each day and were issued a patch labeled with their respective study identifier that was affixed to the sleeve of their Army Combat Uniform (ACU). During the sampling process, the patches were used to identify and track participants as they passed through the chamber. The study identifier was used to document the assignment of sampling pumps and media to a participant along with respective exposure duration.

The BOLC trainees formed ad hoc groups of approximately 20 personnel after receiving a safety briefing and introductory training from the staff operating the CS chamber. The groups formed two lines of ten as the trainees were queued to enter the chamber (Figure 2). Participants were identified by their study identifier patch and outfitted with sampling trains while forming a line to enter the chamber.

Prior to the start of the MCT event, the two chamber operators generated a concentration of CS inside the chamber using a Sterno® can and lighter to heat the CS capsules on an inverted tin can (Appendix B). As a group entered the chamber, the

preceding group assembled at the chamber entrance, and another group moved from the bleacher area to the chamber area. Trainees entered the chamber in groups of 20 wearing military protective masks and the ACU, which includes a long sleeved blouse, pants, and boots. The hands and areas of the neck and head not covered by the protective mask were exposed. After entering the chamber, the operators ensured each individual's mask was functioning properly. Then the trainees were directed to perform a variety of tasks to verify the fit of the protective mask including looking side-to-side, chewing, speaking, and running in place. Upon completion of these exercises, the trainees were directed to remove their masks in groups of two and to repeat a phrase prior to exiting the chamber. The process was repeated until all personnel had exited the chamber. A chamber operator then added additional CS capsules after which the next group was directed to enter the chamber. The process was repeated until all personnel had completed the exercise.

Inside the CS chamber an investigator documented entry and exit times of participants and ensured sampling equipment was functioning. The time sampling pumps were turned on and off was documented. In addition, each MCT iteration was video recorded to enable an accurate accounting of the amount of time individuals were inside the MCT chamber along with respective elapsed time in the chamber after removing the protective mask.

Upon exiting the chamber, the sampling train and study identifier patch were removed from participants. Sample media was capped and placed into a re-sealable plastic bag with the participant's study identifier patch ensuring each sample was assigned properly. Field data sheets and calibration information were synchronized using

the OVS identification number and participant study identifier. Two field blanks per MCT iteration and two trip blanks per iteration were included with the samples. The media was stored in a cooler or refrigerated prior to shipment to the U.S. Navy CIHL lab for analysis.

DATA ANALYSIS

Dataset

The pre- and post-exposure data from the questionnaires and quantified exposure concentrations were linked by participant study identifier and transcribed into spreadsheets to generate the analysis dataset. All survey data were coded for analysis and entered using double entry. A study participant was initially included if all questionnaires were completed and CS exposure concentration was quantified. The linked data was aggregated into a single dataset and imported into both SPSS 22 and STATA 13.1 for analysis (29; 48). STATA was used for exact logistic regression and contingency table analysis using Fisher's exact test of independence, and SPSS was used for the other analyses.

Respiratory outcomes were identified in the study population with the Jackson Method criteria at the three points they were measured. Pre-exposure symptom severity scores were summed individually for each participant to establish baseline symptom severity. Participants were excluded from the analysis if case criteria were met prior to CS exposure since those individuals were not at risk of developing new-onset symptoms. Net symptom scores were calculated by subtracting the 24-hour and one-week post-exposure scores respectively from baseline scores for each participant. Those with a

score greater than five and self-reporting the presence of a cold were identified as cases indicating presence of acute respiratory illness symptoms.

Analysis

Descriptive statistics were used to characterize CS exposure concentrations, study population attributes, and respiratory outcomes meeting case criteria. The distributions of CS concentrations, individual time in chamber, and time out of mask were evaluated for normality using the Shapiro-Wilk test. The independent samples t-test was used to assess the homogeneity of the mean CS concentration between day of MCT and between cases and non-cases. The Kruskal-Wallis test was used to assess the difference in participant time in chamber and time out of mask between the three days of MCT. The difference of mean time in chamber and mean time out of mask between cases and non-cases was evaluated with the Mann-Whitney U test.

The relationship between new-onset cases and exposure concentration was evaluated with exact logistic regression due to the small sample size and case frequency. Participant CS exposure concentration was evaluated as a predictor of respiratory outcomes meeting case criteria (dichotomous) as assessed 24-hours and one week post-exposure separately. Adjustment for demographic and other variables was dependent on sample size and caseload. As a secondary outcome of CS exposure, linear regression was used to evaluate the association between CS exposure concentration and post-exposure net symptom severity scores measured 24-hours and one-week post-MCT.

Case dependence on CS exposure concentration was evaluated by categorizing participants into one of two groups by a threshold concentration. Individuals were categorized into threshold concentration groups using the IDLH (2.00 mg/m^3), one and a

half times the IDLH (3.00 mg/m^3) and twice the IDLH (4.00 mg/m^3). Using each threshold separately, participants were categorized into either the above threshold group or the below threshold group in a contingency table. Fisher's exact test was used to assess the dependence of case status on the respective exposure thresholds because cells in each of the contingency tables had values less than five which violated an assumption of the Chi-squared test of independence. The analysis was repeated separately for cases identified 24-hours and one-week post-exposure.

Potential confounding of the relationship between above threshold CS exposure and respiratory outcomes was evaluated in three steps. Fisher's exact test of independence was used to determine if any study population attributes among those with below threshold exposure were independently associated with case status, the tests were completed separately for participants with exposure below the 3.00 mg/m^3 and 4.00 mg/m^3 thresholds. Then study population attributes were tested for dependence on exposure above the 3.00 mg/m^3 and 4.00 mg/m^3 thresholds separately. If a covariate was associated with the outcome and with over-threshold exposure, it was evaluated to determine if it was an intermediate in the relationship between CS exposure and symptoms of acute respiratory illness. The potential for effect modification was assessed by stratifying the threshold groups by history of respiratory allergies and history of asthma separately to determine if the stratum specific measures of effect were different when compared with the crude measure of association.

In a separate analysis, participants were categorized into one of four exposure groups by exposure concentration to evaluate the association of the CS exposure ranges with symptoms meeting case criteria as evaluated at 24-hours and one-week post-

exposure. Groups were based on the IDLH value of 2.00 mg/m^3 and included: less than 2.00 mg/m^3, 2.00 mg/m^3 to 2.99 mg/m^3, 3.00 mg/m^3 to 3.99 mg/m^3, and greater than 3.99 mg/m^3. The difference in the proportion of cases in each exposure group was evaluated with contingency tables using Fisher's exact test to determine if case status was dependent on exposure grouping because some cell values were less than five. All exposure groups were also compared to each other sequentially in two by two contingency tables to evaluate the dependence of case status between the four groups separately.

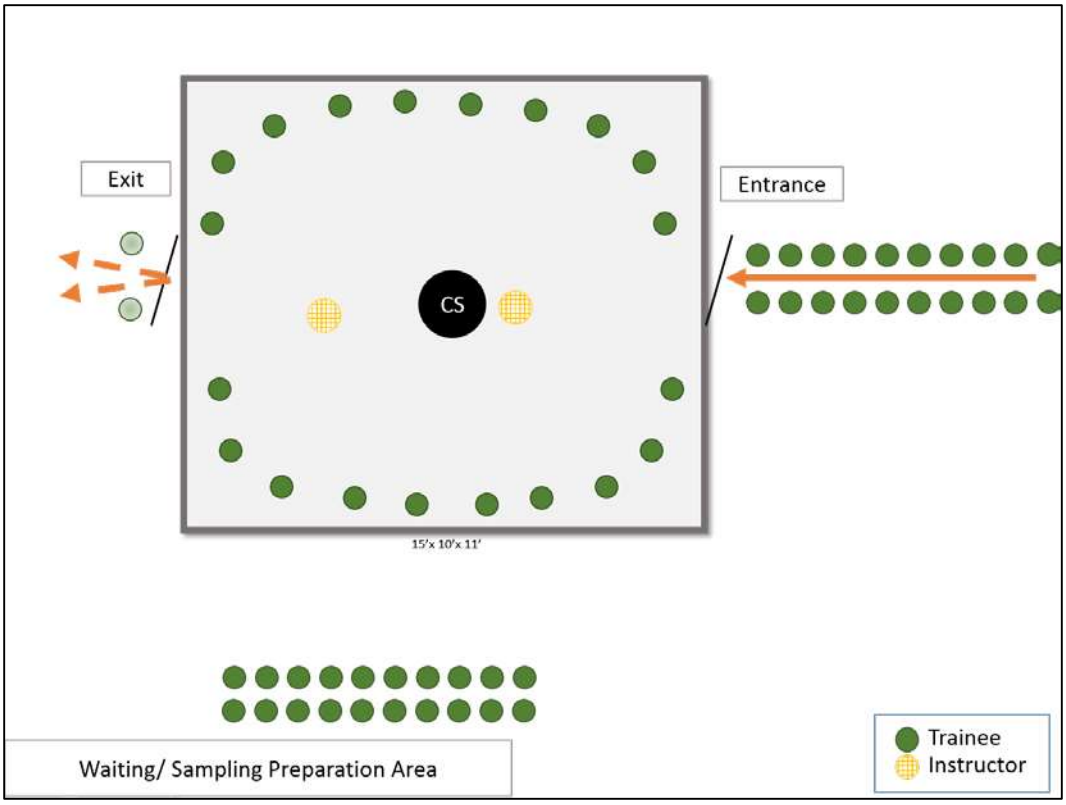

Figure 2. Mask Confidence Training Schematic

Figure 3. OSHA Versatile Sampler (OVS)
(45)

CHAPTER 3: RESULTS

RESPONSE RATE

Of the 546 trainees in the BOLC class followed in this study, 91 (17%) volunteers were enrolled. Participants were included in the analysis if the individual had completed each of the three questionnaires and had CS exposure sampled; seven of the participants did not meet these criteria. Three participants were unavailable when the final survey was administered due to training requirements. CS exposure was not assessed for one participant, and three were removed from the study due to not meeting criteria for a concurrent study. Additionally, CS samples for four participants were excluded due to post-sampling calibration flow rates of more than five percent greater than the pre-sampling flow-rate. Of those meeting the inclusion criteria, six were excluded from the analysis due to meeting case criteria prior to MCT. As a result, of the 91 participants enrolled in the study, 80 (15%) were initially included, and 74 (14%) were considered in the analysis (Figure 4).

BASELINE CHARACTERISTICS

The baseline characteristics of the study population are presented in Table 1 and Table 2. Participants included 36 (49%) males, 38 (51%) females, and a mean age of 26 (±5.4) years. The majority were either physicians or in the midst of completing medical school (77%). The remainder consisted of dentists (8%), nurses (3%), physician's assistants (3%), and veterinarians (10%). Participants were assigned to both training companies, which were each comprised of three platoons. Alpha Company, made up of 1st, 2nd, and 3rd platoons, had 33 (45%) participate in the study. Bravo Company, consisting of 4th, 5th, and 6th platoons, had 41 (55%) participate in the study. Fourth

platoon had the most participate with 19 individuals (26%) while the distribution of participants from the other five platoons was similar with a range of nine to fourteen (12-19%).

A history of respiratory allergies was reported by 14 (19%) individuals, and four (5%) reported a history of asthma. No one in the group was a current smoker, four (5%) had smoked at some point in the past, and the mean BMI in the group was 24.5 (±2.9). The most recent APFT was passed by 20 (27%) with a score in the high range and 17 (23%) did not pass the most recent APFT. The majority (93%) reported less than seven hours of sleep per night in the preceding two weeks. Additionally, contact in the week prior to MCT with a potentially sick individual in the same platoon was reported by 44 (60%) and contact with a sick individual staying in the same tent was reported by 40 (54%). Ten participants (14%) had completed MCT (been exposed to CS) at least once in the past. Four (5%) reported not taking any breaths after removing the protective mask in the CS chamber while 38 (51%) reported taking multiple unprotected breaths.

CS EXPOSURE RESULTS

CS exposure concentration was documented with personal breathing zone samples collected for the 74 individuals included in the analysis. Participants completed MCT with their respective platoons: 21 (28%) on July 14th, 30 (41%) on July 15th, 23 (31%) on July 16th. The overall mean exposure in the study population was 2.75 mg/m^3 (±1.01) however, as depicted in Figure 5, each daily mean concentration differed significantly from the other ($p = < 0.01$) increasing from 1.65mg/m^3 (±0.36) on the first day to 3.58mg/m^3 (±0.94) on the final day (Table 2). Additionally, the individual sample concentrations were normally distributed ($p = 0.94$), the TLV-C [skin] was exceeded in 72

(97%) of participants, and the IDLH was exceed in 51 (69%) of participants. Furthermore, 34 (46%) were exposed to more than one and half the IDLH and eight (11%) were exposed to more than twice the IDLH (Table 3). Time in chamber and time out of mask were not normally distributed. The mean time in the chamber was 5.53 minutes (±1.4) and there was a significant difference of time in chamber between the second and third day (p= 0.049). The mean time out of mask was 8 seconds (± 2) and did not differ by day of exposure (p= 0.53).

RESPIRATORY OUTCOME RESULTS

The primary outcome was new-onset self-reported symptoms of acute respiratory illness meeting case criteria assessed separately at 24-hours and one-week following MCT. Two new-onset cases (3%) were identified 24 hours after exposure and four cases (5%) were identified at one week post-exposure. Symptoms sufficient to meet case criteria occurred in individuals exposed to greater than 3.00 mg/m^3; mean exposure was 3.90 mg/m^3 (±0.99) at the 24-hour follow-up and 3.95 mg/m^3 (±0.65) at the one-week post-exposure follow-up point (Table 4). One individual meeting case criteria after 24 hours also met criteria one week after exposure. The rate of respiratory outcomes during the one-week follow up period was 5.4 cases per 100 person-weeks. The mean CS exposure differed significantly between cases and non-cases identified at one-week post-MCT (p= 0.03), but not for cases identified at the 24-hour follow-up (p= 0.32) which may be due insufficient statistical power (41%). Among the individuals meeting case criteria one-week post-MCT, three of four had symptoms lasting three or more days when reporting at the one-week follow-up (p= 0.02), and three of four reported using cold medication in the one-week follow-up period (p= < 0.01).

Univariate analysis of individual CS exposure as a continuous variable and its association with symptoms meeting case criteria is presented in Table 5. Exact logistic regression was used to assess the CS concentrations measured for study participants as a predictor of respiratory outcomes meeting case criteria identified at both points of follow-up after MCT. CS exposure concentration was associated with increased odds of meeting case criteria at one-week post-MCT with an odds ratio of 5.6 (95% CI 1.3-36.9). Thus a 1.00 mg/m^3 increase in exposure was associated with over five times greater odds of symptoms meeting case criteria one week after MCT. The association between CS exposure concentration and cases identified at the 24-hour post-MCT point was not significant but resulted in a similar odds ratio of 5.7 (95% CI 0.9-82.3). Adjustment for covariates was not feasible due to the sample size and quantity of cases.

Univariate exact logistic regression using a dichotomous predictor value derived from exposure above or below a threshold concentration found the odds of meeting case criteria one week post-MCT were greater with exposure above the 3.00mg/m^3 (OR 6.7; 95% CI 0.8-Inf) and the 4.00mg/m^3 (OR 10.0; 95% CI 0.6- 161.8) thresholds but each finding lacked statistical significance. Similar results occurred between over threshold exposure and cases identified at 24-hours post-MCT (3.00 mg/m^3: OR 2.9 (95%CI 0.2-Inf); 4.00 mg/m^3: OR 8.8 (95%CI 0.1-740.5))

Cases identified at one-week post-MCT were further analyzed for dependence on exposure concentration (Table 6). Participants were categorized into dichotomous threshold groups based on individual exposure concentration using the IDLH value (2.00 mg/m^3), one and a half IDLH (3.00 mg/m^3), and twice IDLH (4.00 mg/m^3). Cases identified at 24-hours post-MCT were independent of exposure above each of the

assessed thresholds. Increased risk of respiratory outcomes did not occur in the study population in the 24-hour period following CS exposure.

Among cases identified at the follow-up one week post-MCT, case status was independent of exposure at the 2.00 mg/m^3 threshold (p= 0.30) (Table 6). Case status was dependent on exposure above the 3.00 mg/m^3 threshold (p= 0.04) however no cases occurred below this level precluding the measure of relative effect. Those exposed to levels above the 3.00 mg/m^3 threshold had 11.8% (95% CI 0.9 – 22.6) excess risk compared to those with below threshold exposure. Case status was dependent on exposure above the 4.00 mg/m^3 threshold with 8.3 times greater risk (p= 0.055) of developing symptoms meeting case criteria compared to those exposed to less than 4.00 mg/m^3, although the finding was not significant at the α= 0.05 level of significance.

Using individual exposure concentrations the 74 participants were also categorized into one of four exposure groups that were based on increasing derivations of the IDLH concentration (Table 7). Those meeting case criteria among the exposure groups at one-week post-exposure were associated with the two higher concentration exposure groups (p= 0.04). Symptoms sufficient to meet case criteria occurred in participants in the 3.00 – 3.99 mg/m^3 and greater-than 3.99 mg/m^3 groups. No association was present among exposure groups in the proportion meeting case criteria at the 24-hour post-exposure follow-up (p= 0.20).

The 3.00 – 3.99 mg/m^3 group was used as the referent group when assessing the risk of developing symptoms sufficient to meet case criteria in the greater than 3.99 mg/m^3 exposure group because cases were present in both groups. The greater than 3.99 mg/m^3 exposure group had 3.3 (95%CI: 0.5-19.5) times greater risk of developing

symptoms meeting case criteria. The finding was not significant (p= 0.23) thus case status was independent of exposure group when making the comparison between the other exposure groups.

The linear relationship between CS exposure and symptom scores at 24-hours post-exposure and one-week post-exposure was evaluated. A linear association was present between CS concentration and one week post-exposure symptom scores (p= 0.04) however, exposure may only explain 6% of the variability in post-exposure symptom severity scores ($R^2 = 0.06$). A linear association was not present between CS Concentration and 24-hour symptom scores (p= 0.20).

Cases identified one-week post-exposure were exposed to a significantly higher CS concentration than non-cases (p= 0.03). The median time in chamber (p= 0.57) and time out of mask (p= 0.95) did not differ between cases and non-cases. The association between exposure above the 3.00 mg/m^3 threshold and covariates in the study was also evaluated. Exposure above the threshold concentration of 3.00 mg/m^3 (1.5x IDLH) was dependent on date of MCT (p= < 0.01) and Platoon (p= < 0.01). The same associations were present with exposure above the 4.00 mg/m^3 threshold concentration and date of MCT (p= < 0.01) and Platoon (p= < 0.01).

The association between cases and covariates in the study was evaluated with contingency tables. Meeting case criteria was associated with reports of greater than moderate allergy symptoms (p= 0.03), being awakened from sleep by their own coughing (p= < 0.01), and reporting a reduction in capacity for vigorous physical activity after MCT (p= 0.01). Potential confounders were tested for an independent association with case status among the below 4.00 mg/m^3 threshold group. Those reporting a history of

respiratory allergies were associated with meeting case criteria (p= 0.04) while those reporting a history of smoking and asthma were not associated with meeting case criteria. Since history of respiratory allergies was not associated with exposure above either threshold concentration, it did not meet confounding criteria in the study.

Stratification by self-reported history of respiratory allergies was used to evaluate if the condition modified the observed effect between respiratory outcomes and CS exposure above the 4.00 mg/m^3 threshold (Table 8). Meeting case criteria was dependent on exposure above 4.00 mg/m^3 (p= 0.01) among those without a history of respiratory allergies but not among those with a history of respiratory allergies. The cases with exposure below 4.00 mg/m^3 reported a history of respiratory allergies while cases with exposure greater than 4.00 mg/m^3 did not have a history of respiratory allergies.

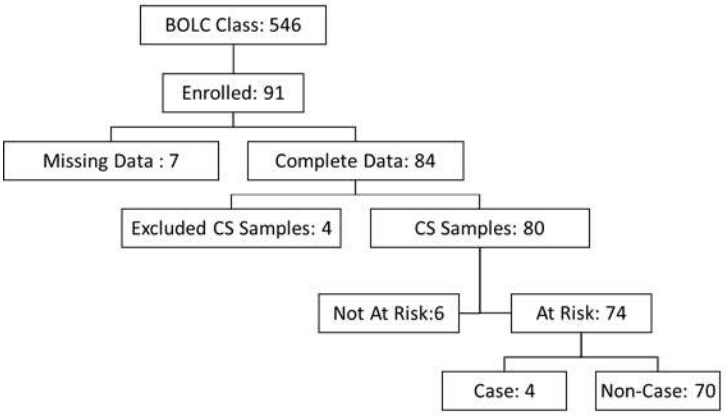

Figure 4. Study Population

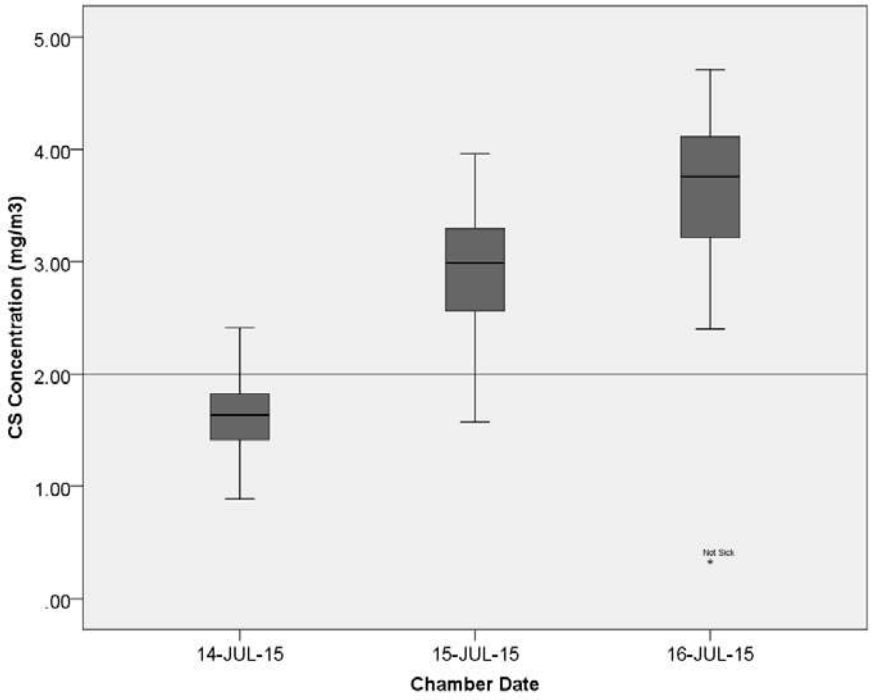

Figure 5. Mean CS Exposure Concentration by Date

Table 1. Characteristics of Study Participants

Characteristics *(n=74)*		**n**	**%**
History of Asthma		4	5.4
History of Allergies		14	18.9
Prior contact with sick individual			
	Platoon	44	59.5
	Tent	40	54.1
Past Smoker		4	5.4
Current Smoker		0	0.0
< 7 hours of sleep/night in last week		69	93.2
Gender			
	Male	36	48.6
	Female	38	51.4
Physical Fitness Test			
	< 180	17	23.0
	180-269	37	50.0
	>269	20	27.0
Prior CS Exposure			
	Never	64	86.5
	One Time	5	6.8
	> One Time	5	6.8
Chamber Date			
	14-Jul-15	21	28.4
	15-Jul-15	30	40.5
	16-Jul-15	23	31.1
Breaths taken without respirator			
	No Breaths	4	5.4
	One Breath	32	43.2
	≥ One Breath	38	51.4
Training Company			
	A Company	33	44.6
	B Company	41	55.4
Training Platoon			
	1st Platoon	10	13.5
	2nd Platoon	11	14.9
	3rd Platoon	11	14.9
	4th Platoon	19	25.7
	5th Platoon	9	12.2
	6th Platoon	14	18.9

Branch Specialty			
	Dental	6	8.1
	Medical	25	33.8
	Medical Service	32	43.2
	Medical Specialist	2	2.7
	Nurse	2	2.7
	Veterinary	7	9.5

Table 2. Characteristics of Study Participants (continuous variables)

Characteristics *(n=74)*		**mean**	**sd**
Age		26.5	5.4
BMI		24.5	2.9
Time in Chamber *(min.)*	Overall	5:32	1:24
	14-Jul-15	5:42	0:41
	15-Jul-15	5:52	1:19
	16-Jul-16	4:58	1:48
CS Concentration *(mg/m^3)*	Overall	2.75	1.01
	14-Jul-15	1.65	0.36
	15-Jul-15	2.88	0.63
	16-Jul-16	3.58	0.94
Time out of Mask *(seconds)*	Overall	0:08	0:02
	14-Jul-15	0:08	0:03
	15-Jul-15	0:09	0:02
	16-Jul-16	0:09	0:02

Table 3. Exposure Levels Among Participants

Exposure Threshold	**n**	**%**
≥ 0.39 mg/m^3	72	97
≥ 2.00 mg/m^3	51	69
≥ 3.00 mg/m^3	34	46
≥ 4.00 mg/m^3	8	11

Table 4. Respiratory Outcomes Meeting Case Criteria in the Study Period

Outcomes	Cases		Non-cases		At Risk	CS Concentration	
	(n)	*(%)*	*(n)*	*(%)*	*(n)*	*(mean)*	*(sd)*
One-week Post-exposure	4	5.4	70	94.6	74	3.90	0.65
24 Hours Post-exposure	2	2.7	72	97.3	74	3.95	0.99

Table 5. Exact Logistic Regression Analysis of CS Concentration (mg/m^3) as a Predictor of Respiratory Outcomes (univariate)

Respiratory Outcome Follow-up	Cases *(n)*	P Value*	Odds Ratio	(95% CI)
One-week Post-exposure *(Crude)*	4	0.01	5.6	1.3 – 36.9
24-hours Post-exposure *(Crude)*	2	0.08	5.7	0.8 – 82.3

**Fisher's exact test*

Table 6. The Risk of Developing Respiratory Outcomes Meeting Case Criteria in the Over-threshold Group when Compared to the Below-threshold Group

Exposure Threshold	P Value*	Risk Ratio	(95% CI)	Risk Difference	(95% CI)
2.00 mg/m^3	0.303	–	– –	7.8	0.5 – 15.2
3.00 mg/m^3	0.040	–	– –	11.8	0.9 – 22.6
4.00 mg/m^3	0.056	8.3	1.3 – 50.8	22.0	-8.3 – 52.3

**Fisher's exact test*

Table 7. Exposure Concentration Groupings Among Trainees

CS Concentration	Trainees		Cases*
mg/m^3	*n*	*%*	*n*
0 – 1.99	23	31	0
2.00 – 2.99	17	23	0
3.00 – 3.99	26	35	2
> 3.99	8	11	2

**Cases identified one-week after MCT*

Table 8. Association Between Meeting Case Criteria and Threshold Exposure Stratified by History of Respiratory Allergies

History of Respiratory Allergies	Exposure Threshold	Cases *(n)*	P Value*
No Respiratory Allergy History	≥ 4.00 mg/m3	2	0.01
	< 4.00 mg/m3	0	
Respiratory Allergy History	≥ 4.00 mg/m3	0	1.00
	< 4.00 mg/m3	2	

**Fisher's exact test*

CHAPTER 4: DISCUSSION

FINDINGS

The hypothesized association between over-threshold CS exposure and respiratory outcomes was confirmed in the study. New-onset symptoms of acute respiratory illness were associated with CS exposure above 3.00 mg/m^3 when compared to exposure below 3.00 mg/m^3, which suggests the presence of a threshold effect. Moreover, an increase of 1.00 mg/m^3 in individual CS exposure concentration was associated with 5.6 times greater odds (95%CI 1.3-36.9) of developing symptoms of acute respiratory illness one-week after MCT.

The temporal association of new-onset respiratory outcomes with MCT indicates exposure to CS above the IDLH concentration may lead to excess risk of acute respiratory illness in BOLC trainees. The risk of developing new-onset symptoms sufficient to meet case criteria one-week after MCT increased as exposure concentration increased and was dependent on exposure above the threshold concentration of 1.5 times the IDLH (3.00 mg/m^3). Cases occurred among those exposed to CS above this concentration and it was associated with three excess cases per 25 participants compared with those exposed to CS concentrations below 3.00 mg/m^3. Similarly, exposure above the 4.00 mg/m^3 threshold concentration was associated with 8.3 times the risk of developing symptoms meeting case criteria compared with those exposed to less than 4.00 mg/m^3 however, the finding was not significant at the 95% confidence level (p= 0.055). Among those exposed to more than 4.00 mg/m^3, 88% of cases could be attributed to the above-threshold CS exposure concentration compared to those exposed below-threshold. The association between CS exposure above the IDLH value and increased risk of symptoms suggestive of acute respiratory illness was consistent and with the

known adverse health effects of CS and with the findings in similar studies. A history of respiratory allergies may modify the effect between CS exposure above 3.00 mg/m^3 and acute respiratory illness, but a larger sample is necessary to confirm the effect. Similarly, no interaction was apparent between smoking in the past or having a history of asthma and the relationship between over-threshold CS exposure and symptoms of acute respiratory illness, but a larger sample is necessary to determine the generalizability of the finding.

Respiratory outcomes assessed 24 hours after MCT were not associated with CS exposure above either threshold concentration. An increase of 1.00 mg/m^3 in individual CS exposure was associated with 5.7 times greater odds developing symptoms sufficient to meet case criteria but the finding was not significant at the 95% confidence level ($p = 0.08$). The measure of effect was similar to that observed in the population one-week after MCT, which was indicative of cases in the study occurring among those exposed to CS concentrations above 3.00 mg/m^3. The lack of significance may be due to insufficient power and the low frequency of cases in the study or it may indicate 24 hours did not allow enough time for the development of illness.

Associations

The personal breathing zone samples were representative of exposure among the participants; the time spent in the MCT chamber without a protective mask did not differ significantly by day of MCT, between cases and non-cases, or between threshold concentration groups (3.00 mg/m^3 and 4.00 mg/m^3). The daily mean CS concentration during MCT increased each day the training occurred because the MCT chamber operators used more CS capsules each successive day and due to residual CS from MCT

the previous day. Accordingly, exposure above both threshold concentrations was associated with day of MCT and with the platoons that completed MCT on the second and third day. Beyond exposure concentration, those with symptoms sufficient to meet case criteria were associated with reporting a degraded ability to perform vigorous physical activity, being awakened by their own coughing, and more than moderate respiratory allergy symptoms among those with a history of respiratory allergies. Reporting a history of respiratory allergies was also associated with reporting a degraded ability to perform vigorous physical activity in the week after completing MCT. These associations may constitute illness-induced symptoms or be indicative of respiratory tract irritation.

The study population was a relatively young, fit, and sleep deprived group that did not include any current smokers. Several individuals reported a history of asthma and 19% reported a history of respiratory allergies. A history of smoking, asthma, respiratory allergies, and contact with potentially infectious individuals in the population did not meet confounding criteria. Reporting these risk factors was not associated with exposure above either the 3.00 mg/m^3 or 4.00 mg/m^3 threshold concentrations.

The threshold grouping defined by exposure either above or below 4.00 mg/m^3 was used to determine if risk factors were independently associated with meeting case criteria among the unexposed since cases occurred in both the above-threshold and below-threshold groups. Reporting a history of respiratory allergies was independently associated with meeting case criteria among those in the below threshold group (considered unexposed). As a result, the potential risk factor of respiratory allergies may

have acted as an effect modifier in the observed relationship between CS exposure above the 4.00 mg/m^3 threshold and the development of acute respiratory illness symptoms.

Effect Modification

Among new-onset cases in the one-week follow-up period, those with a self-reported history of respiratory allergies developed symptoms meeting case criteria when exposed to lower CS concentrations compared to those without respiratory allergies. When the 4.00 mg/m^3 threshold groups were stratified by history of respiratory allergies, cases in the without respiratory allergies stratum were associated with exposure above the 4.00 mg/m^3 threshold but cases in the with respiratory allergies stratum were not associated with over-threshold exposure. Participants with a history of respiratory allergies who reported symptoms sufficient to meet case criteria were exposed to CS concentrations between 3.00 – 4.00 mg/m^3 and those without a history of respiratory allergies reported symptoms meeting case criteria when exposed to CS above 4.00 mg/m^3. Participants with respiratory allergies may have been more sensitive to CS exposure because they developed symptoms when exposed to lower CS concentrations compared to participants without respiratory allergies. The limited number of cases and sample size precluded analysis of the magnitude of this potential effect.

Similar Studies

Some new-onset cases could have occurred despite CS exposure since the background rate of acute respiratory illness in the study population was unknown. A study of self-reported acute respiratory illness in a military population found a rate of 3.45 cases per 100 person-weeks while the rate of post-exposure cases in this study was

5.4 per 100 person-weeks (47). When compared using a rate ratio, a 59% higher rate of illness occurred in the post-MCT BOLC trainees.

The association between above-OEL CS exposure and post-MCT respiratory outcomes was similar to previous findings but the comparison between the rates of respiratory outcomes in the week before with the week after MCT were different (28). In this study, the estimated rate ratio of cases in the week after MCT when compared to the week before MCT was 0.7 (95%CI 0.2 – 2.6) which indicates no difference among participants meeting case criteria in the week before MCT and the week following MCT. The overall pre/post MCT acute respiratory illness rate ratios observed in the studies by Hout et al., 2.44 (95%CI 1.23 – 3.43) and 1.79 (95%CI 1.29 – 2.47), were higher compared to the rate observed in this study (27; 28). Consequently, respiratory outcomes in this study may not have been related to CS exposure. However, the comparison of outcomes between threshold groups indicates it was unlikely the cases occurred at exposure concentrations above 3.00 mg/m^3 only by chance. Therefore, further research is necessary to confirm the results of this study.

The evaluation of the relationship between MCT and acute respiratory illness by Hout et al. found an increased risk of acute respiratory illness when CS exposure exceeded the TLV-C, and it was hypothesized that a threshold effect between exposure and acute respiratory illness in the study population occurred between 0.00 – 2.00 mg/m^3 (27). The distribution of CS concentrations in this study had a different range of exposure, 0.33 – 4.71 mg/m^3, compared with exposures found in the study by Hout et al., which ranged from 0.26 – 55.24 mg/m^3 in one study and from 0.05 – 2.22 mg/m^3 in the follow up study (27; 28). Nonetheless, a threshold effect was observed in this study,

which occurred at 3.00 mg/m^3 instead of the 2.00mg/m^3 threshold hypothesized by Hout et al.

LIMITATIONS

There are a number of limitations associated with this study. Prospective studies may have nonresponse bias when enrolling volunteers and loss to follow-up could have introduced bias in the relatively small sample. One BOLC class was observed which limited the number of participants and restricted the exposure assessment to three separate iterations of MCT. Additionally, the study was limited to the month of July, which may not be generalizable to classes occurring at different times in the year such as during influenza season since a higher background rate of acute respiratory illness may be present (39; 41; 54). As a result, the association of illness with CS exposure observed in this study may change throughout the year.

The study lacked the sample size and case frequency to create a multivariate model. When evaluating the risk of respiratory outcomes between threshold exposure groups, the sample was also underpowered, and the low frequencies of those reporting a history of smoking, asthma, and respiratory allergies precluded controlling for these factors and the analysis of stratum specific effects.

The primary outcome was detected using a validated self-reporting diagnostic tool in self-administered questionnaires. Hence, cases that met the criteria of an acute respiratory illness in the study were not clinically diagnosed, or confirmed with laboratory testing. Using self-reported respiratory symptom severity could also lead to misclassification of the study outcome or be subject to recall error. The potential misclassification was minimized because the questionnaires addressed health status with

respect to MCT using short recall periods of between 24 hours and one week. Additionally, the self-reporting diagnostic tool requires both the self-report of a cold and symptom severity above a cutoff making it more sensitive compared to only the self-report of a cold. In addition, the number of cases identified through self-reports may over-estimate the number that could be expected seek medical care. However, three of the four cases reported taking cold medications and one sought medical care within the one-week follow-up period. It was also possible that social desirability may have biased self-reported weight, height, or previous APFT score, however each questionnaire was self-administered and confidential thus it was not necessary for participants to reveal information directly.

The self-reporting tool used to identify respiratory outcomes may not fully capture the adverse health effects arising from CS exposure such as irritation of the respiratory tract since it was validated in studies of common cold viruses (25). If present, irritation induced by exposure could reasonably be expected in the 24 hours following MCT however, respiratory outcomes meeting case criteria were not associated with exposure above either threshold concentration at the 24-hour post-MCT follow-up (31; 43). The lack of a statistical difference between mean CS exposure of those meeting and not meeting case criteria at 24 hours after MCT was likely due to the low frequency of cases ($1-\beta = 41\%$). The mean symptom severity scores of all participants reported 24 hours after MCT were higher than the baseline and significantly higher than one-week post-MCT scores. This was a possible indication of elevated (above baseline) respiratory irritation lasting at least 24 hours after MCT that was not associated with illness. Although, it was not possible to determine if symptom severity was due to irritation or

infection in the study population, symptoms are an important indication of the impact on post-MCT health regardless of cause.

CHAPTER 5: CONCLUSIONS

The development of symptoms suggestive of acute respiratory illness among BOLC trainees was dependent on CS exposure concentrations greater than one and half times the IDLH value during MCT and the odds of developing symptoms of acute respiratory illness increased as exposure concentration increased. Individual symptom severity was not linked in a useful way to CS exposure concentration. In addition, risk factors assessed in the study did not meet confounding criteria although smoking history and asthma did not occur with enough frequency for the analysis of potential effect on the relationship between MCT and acute respiratory illness symptoms.

This study found results similar to previous studies while using self-reported respiratory outcomes, assessing individual exposure, and documenting individual characteristics and risk factors. The outcome was temporally linked to exposure and a potential threshold effect was identified at a higher concentration than previously postulated. Maintaining the CS concentration below IDLH may reduce the risk of excess acute respiratory illness in a similar recruit population, and it is possible respiratory allergies may predispose a trainee to adverse health effects following CS exposure.

FUTURE RESEARCH

Further research with a larger sample using the same methods to assess exposure and symptoms of acute respiratory illness is necessary to verify results and to explore the potential effect of respiratory allergies. Based on the outcomes of this study a sample size of between 220 and 400 is necessary for sufficient power to evaluate the risk associated with CS exposure while accounting for potential confounders or effect modifiers. Future studies should also be designed to capture rates of acute respiratory

illness in the week prior to MCT and the week after MCT to account for background rate of acute respiratory illness.

APPENDICES

A. Questionnaires

B. MCT Site Photos

C. IRB Authorization Form

D. Consent Form, Information Sheet

E. Guide To Study Variables

F. Association of Select Variables with Case Status

G. Association of Select Variables with Exposure Above 3.00 mg/mg^3

APPENDIX A. QUESTIONNAIRES

1. Pre- Mask Confidence Training Questionnaire
2. 24-Hour Post- Mask Confidence Training Questionnaire
3. One-week Post-Mask Confidence Training Questionnaire

1. Pre-Mask Confidence Training Questionnaire

1. Use the scale below to rate the <u>average severity</u> of your symptoms over <u>the last three (3) days</u>:

(please mark one circle for each symptom)

	Mild Symptoms	Moderate Symptoms	Severe Symptoms	Do not have this symptom
Sneezing	○	○	○	○
Runny Nose	○	○	○	○
Stuffy Nose	○	○	○	○
Sore Throat	○	○	○	○
Cough	○	○	○	○
Headache	○	○	○	○
Feeling Tired	○	○	○	○
Chills	○	○	○	○

2. Do you think that you have a <u>cold</u> or **may be getting a** cold? *(choose one)*

- □ Yes
- □ No
- □ Don't know

3. In the past <u>three (3) days</u>, have you taken medication for any of the following reasons?

<u>Yes</u>	<u>No</u>	
□	□	A cold
□	□	Cough
□	□	Fever
□	□	Runny nose

4. In the past <u>three (3) days</u>, have you gone to sick call for any of the following reasons?

<u>Yes</u>	<u>No</u>	
□	□	A cold
□	□	Cough
□	□	Fever
□	□	Runny nose

5. Has a doctor or other health professional ever told you that you have respiratory allergies?
(choose one)

- □ Yes
- □ No
- □ Don't know

6. According to the scale below, please rate the <u>average severity</u> of your respiratory allergies over the past <u>three (3) days.</u> *(choose one)*

- □ I don't have respiratory allergies

Very Mild	Mild	Moderate	Severe	Very Severe	No Symptoms
○	○	○	○	○	○

7. Have you used any medications to ease your respiratory allergies in the past <u>three (3) days</u>?
(choose one)

- □ I don't have respiratory allergies
- □ Yes
- □ No

8. Has a doctor or other health professional ever told you **that you have asthma?**
(choose one)

- □ Yes
- □ No
- □ Don't know

9. According to the scale below, please rate the average severity of your asthma symptoms in the past <u>three (3) days</u>. *(choose one)*

- □ I don't have asthma

Very Mild	Mild	Moderate	Severe	Very Severe	No Symptoms
○	○	○	○	○	○

10. Have you used any medication(s) or an inhaler to control your asthma symptoms in the past <u>three (3) days</u>? *(choose one)*

- □ I don't have asthma
- □ Yes
- □ No

11. In the past <u>year</u>, how many days did you miss work or school due to respiratory illness? *(choose one)*

- □ No days missed
- □ 1 or 2 days missed
- □ 3 or more days missed

12. In the <u>past week</u>, has your roommate had <u>any</u> of the following: a cold, cough, fever, or runny nose? *(choose one)*

- □ Yes
- □ No
- □ Don't know
- □ No Roommate

13. In the <u>past week</u>, has anybody in your platoon had <u>any</u> of the following: a cold, cough, fever, or runny nose? *(choose one)*

- □ Yes
- □ No
- □ Don't know

14. Since arriving at Camp Bullis, has anybody staying in your tent had <u>any</u> of the following: a cold, cough, fever, or runny nose? *(choose one)*

- □ Yes
- □ No
- □ Don't know

15. On average, about how many hours of sleep <u>per night</u> did you get in the past <u>two weeks</u>? *(choose one)*
[Seep is defined from the time you laid down until the time you got out of bed, minus any time intentionally spent awake (example: watching TV)]

- □ Less than 7 hours of sleep
- □ 7 hours of sleep or more

16. Have you smoked at least 100 cigarettes in your <u>entire life</u>? *(choose one)*

- □ Yes
- □ No
- □ Don't know

17. Do you <u>now</u> smoke cigarettes every day, some days or not at all? *(choose one)*

- □ Every day
- □ Some Days
- □ Not at all

18. Have you <u>ever</u> been exposed to CS gas during a military mask confidence training exercise?
(choose one)

- □ Yes, more than one time
- □ Yes, one time
- □ No, I have never completed Mask Confidence Training

19. Age _____

20. Gender

- □ Male
- □ Female

21. Height: _____ feet _____ inches

22. Weight: _____ pounds

23. What was your most recent Army Physical Fitness Test (APFT) Score? *(choose one)*

- □ Less than 180
- □ 180 - 269
- □ 270 or greater
- □ I have not taken an APFT

24. What is your branch of service in the Army Medical Department (AMEDD)?

- □ Dental Corps (DC)
- □ Medical Corps (MC)
- □ Medical Service Corps (MS)
- □ Medical Specialist Corps (SP)
- □ Nurse Corps (AN)
- □ Veterinary Corps (VC)
- □ Other_____

25. To which Company are you assigned while completing BOLC? *(choose one)*
(This refers to your BOLC Company (not A Co. 187th Med BN).

- □ A Company
- □ B Company
- □ C Company
- □ D Company
- □ Other_____

26. To which Platoon are you assigned while completing the BOLC? *(choose one)*

- □ 1st Platoon
- □ 2nd Platoon
- □ 3rd Platoon
- □ 4th Platoon
- □ Other_____

2. 24-Hour Post-Mask Confidence Training Questionnaire

1. **After removing your protective mask while <u>in</u> the CS chamber, about how many times did you take a breath prior to leaving the chamber?** *(choose one)*

   - □ I did not remove my mask.
   - □ I did not take any breaths.
   - □ I took one (1) breath.
   - □ I took two (2) or more breaths.

2. **How much physical discomfort did you experience while you were <u>in</u> the CS chamber?** *(choose one)*

Very Mild Discomfort	Mild Discomfort	Moderate Discomfort	Severe Discomfort	Very Severe Discomfort
○	○	○	○	○

3. **<u>After exiting</u> the CS chamber, approximately how long did it take for the effects from breathing the CS gas to stop?** *[Stop – means that your symptoms eased to the point you could easily see, you were no longer coughing, and your nose stopped running.] (choose one)*

   - □ Less than 30 minutes
   - □ 30 minutes to 1 hour
   - □ Greater than 1 hour
   - □ Did not experience any symptoms
   - □ Don't know

4. **Use the scale below to rate the <u>average severity</u> of your symptoms in the 24-hour period <u>after</u> going through the CS chamber EXCLUDING that first hour.**

(please mark one circle for each symptom)

	Mild Symptoms	Moderate Symptoms	Severe Symptoms	Do not have this symptom
Sneezing	○	○	○	○
Runny Nose	○	○	○	○
Stuffy Nose	○	○	○	○
Sore Throat	○	○	○	○
Cough	○	○	○	○
Headache	○	○	○	○
Feeling Tired	○	○	○	○
Chills	○	○	○	○

5. **Do you think that you have a <u>cold</u> or may be getting a cold?** *(choose one)*

   □ Yes
   □ No
   □ Don't know

6. **In the 24-hour period <u>after</u> going through the CS chamber EXCLUDING that first hour, have you taken medication for <u>any</u> of the following reasons?**

Yes	No	
□	□	A cold
□	□	Cough
□	□	Fever
□	□	Runny nose

7. **In the 24-hour period <u>after</u> going through the CS chamber EXCLUDING that first hour, have you gone to sick call for <u>any</u> of the following reasons?**

Yes	No	
□	□	A cold
□	□	Cough
□	□	Fever
□	□	Runny nose

8. **Use the scale below to rate the <u>average severity</u> of your symptoms in the 24-hour period <u>after</u> going through the CS chamber EXCLUDING that first hour.**

(please mark one circle for each symptom)

	Very Mild Symptoms	Mild Symptoms	Moderate Symptoms	Severe Symptoms	Very Severe Symptoms	Do not have this symptom
Tightness of the chest	○	○	○	○	○	○
Shortness of breath	○	○	○	○	○	○
Difficulty breathing	○	○	○	○	○	○
Sudden feeling of suffocation	○	○	○	○	○	○
Wheezing	○	○	○	○	○	○

9. In the 24-hour period <u>after</u> going through the CS chamber EXCLUDING that first hour, have you experienced <u>any</u> of the following?

Yes	No	
□	□	Skin irritation *(on head, neck, and/or hands)*
□	□	Burning sensation *(on head, neck, and/or hands)*
□	□	Rash *(on head, neck, and/or hands)*
□	□	Upset Stomach
□	□	Heartburn
□	□	Nausea
□	□	Vomiting
□	□	Diarrhea

10. In the 24-hour period after going through the CS chamber EXCLUDING that first hour, have you noticed any change in your capacity for vigorous physical activity*?* *(choose one)*
[Examples of vigorous physical activity include jogging or bicycling uphill]

Much Better	Somewhat Better	About the Same	Somewhat Worse	Much Worse
○	○	○	○	○

11. Please rate the <u>average severity</u> of your respiratory allergies in the 24-hour period <u>after</u> going through the CS chamber EXCLUDING that first hour. *(choose one)*

□ I don't have respiratory allergies

Very Mild	Mild	Moderate	Severe	Very Severe	No Symptoms
○	○	○	○	○	○

12. Have you used any medication to ease your respiratory allergies in the 24-hour period <u>after</u> going through the CS chamber EXCLUDING that first hour? *(choose one)*

□ I don't have respiratory allergies
□ Yes
□ No

13. Please rate the <u>average severity</u> of your asthma symptoms in the 24-hour period <u>after</u> going through the CS chamber EXCLUDING that first hour. *(choose one)*

□ I don't have asthma

Very Mild	Mild	Moderate	Severe	Very Severe	No Symptoms
○	○	○	○	○	○

14. Have you used any medication or an inhaler to control your asthma symptoms in the 24-hour period <u>after</u> going through the CS chamber EXCLUDING that first hour? *(choose one)*

- □ I don't have asthma
- □ Yes
- □ No

15. Do you have any additional symptoms or health concerns related to going through the CS chamber?

3. One-week Post-Mask Confidence Training Questionnaire

16. Use the scale below to rate the <u>average severity</u> of your symptoms in the week AFTER going through the CS chamber EXCLUDING the first 24-hours after the event.

(please mark one circle for each symptom)

	Mild Symptoms	Moderate Symptoms	Severe Symptoms	Do not have this symptom
Sneezing	○	○	○	○
Runny Nose	○	○	○	○
Stuffy Nose	○	○	○	○
Sore Throat	○	○	○	○
Cough	○	○	○	○
Headache	○	○	○	○
Feeling Tired	○	○	○	○
Chills	○	○	○	○

17. If you had any of the symptoms that were listed in the previous question, about when did they begin?

- □ No symptoms
- □ 0-2 Days ago
- □ 3-6 Days ago

- □ Other_____

18. Did any of the following symptoms last for <u>three (3)</u> days or longer in the <u>week</u> after going through the CS chamber?

- □ No symptoms

<u>Yes</u>	<u>No</u>	
□	□	A cold
□	□	Runny Nose
□	□	Cough
□	□	Fever

19. Do you think that you had a cold in the <u>week</u> after going through the CS chamber EXCLUDING the first 24-hours after the event? *(choose one)*

- □ Yes
- □ No
- □ Don't know

20. Have you taken <u>medication</u> for any of the following reasons in the <u>week</u> after going through the CS chamber EXCLUDING the first 24-hours after the event?

Yes	No	
□	□	A cold
□	□	Cough
□	□	Fever
□	□	Runny nose

21. Have you gone to <u>sick call</u> for any of the following reasons in the <u>week</u> after going through the CS chamber EXCLUDING the first 24-hours after the event?

Yes	No	
□	□	A cold
□	□	Cough
□	□	Fever
□	□	Runny nose

22. Do you think that you have a cold or may be getting a cold now? *(choose one)*

- □ Yes
- □ No
- □ Don't know

23. Use the scale below to rate the <u>average severity</u> of your symptoms in the <u>week</u> after going through the CS chamber EXCLUDING the first 24-hours after the event:

(please mark one circle for each symptom)

	Very Mild Symptoms	Mild Symptoms	Moderate Symptoms	Severe Symptoms	Very Severe Symptoms	Do not have this symptom
Tightness of the chest	○	○	○	○	○	○
Shortness of breath	○	○	○	○	○	○
Difficulty breathing	○	○	○	○	○	○
Sudden feeling of suffocation	○	○	○	○	○	○
Wheezing	○	○	○	○	○	○

24. Have you experienced <u>any</u> of the following conditions in the <u>week</u> after going through the CS chamber EXCLUDING the first 24-hours after the event?

Yes	No	
□	□	Skin irritation *(on head, neck, and/or hands)*
□	□	Burning sensation *(on head, neck, and/or hands)*

□ □ Rash *(on head, neck, and/or hands)*
□ □ Upset Stomach
□ □ Heartburn
□ □ Nausea
□ □ Vomiting
□ □ Diarrhea

25. Have you been awakened from sleep by your own coughing in the <u>week</u> after going through the CS chamber EXCLUDING the first 24-hours after the event? *(choose one)*

□ Yes
□ No
□ Don't know

26. Have you noticed any change in your capacity for vigorous physical activity in the <u>week</u> after going through the CS chamber EXCLUDING the first 24-hours after the event? *(choose one)*
(Examples of vigorous physical activity include jogging or bicycling uphill)

Much Better	Somewhat Better	About the Same	Somewhat Worse	Much Worse
○	○	○	○	○

27. Please rate the <u>average severity</u> of your respiratory allergies in the <u>week</u> after going through the CS chamber EXCLUDING the first 24-hours after the event. *(choose one)*

□ I don't have respiratory allergies

Very Mild	Mild	Moderate	Severe	Very Severe	No Symptoms
○	○	○	○	○	○

28. Have you used medication to ease your respiratory allergies in the <u>week</u> after going through the CS chamber EXCLUDING the first 24-hours after the event? *(choose one)*

□ I don't have respiratory allergies
□ Yes
□ No

29. Please rate the <u>average severity</u> of your asthma symptoms in the <u>week</u> after going through the CS chamber EXCLUDING the first 24-hours after the event. *(choose one)*

□ I don't have asthma

Very Mild	Mild	Moderate	Severe	Very Severe	No Symptoms
○	○	○	○	○	○

30. Have you used any medication or an inhaler to control your asthma symptoms in the <u>week</u> after going through the CS chamber EXCLUDING the first 24-hours after the event? *(choose one)*

□ I don't have asthma
□ Yes
□ No

31. On average, about how many hours of sleep <u>per night</u> did you get in the past <u>week</u>? *(choose one) [Sleep is defined from the time you laid down until the time you got out of bed, minus any time intentionally spent awake (example: watching TV)]*

□ Less than 7 hours of sleep
□ 7 hours of sleep or more

32. Do you have any additional symptoms or health concerns related to going through the CS chamber?

APPENDIX B. SITE PHOTOS

Figure B-1. MCT Chamber Entrance

Figure B-2. MCT Chamber Exit

Figure B-3. BOLC Trainees Removing Masks Prior to Exiting the MCT Chamber

Figure B-4. CS Capsule Heating Device

APPENDIX C. IRB AUTHORIZATION

UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES
4301 JONES BRIDGE ROAD
BETHESDA, MARYLAND 20814-4712
http://www.usuhs.mil

July 02, 2015

MEMORANDUM FOR CPT MATTHEW J. HOLUTA, MSC, USA, PREVENTIVE MEDICINE AND BIOSTATISTICS

SUBJECT: USU IRB #1 (FWA 00001628; DoD Assurance P60001) Approval of Protocol TO-87-3564 for Human Subjects Participation

Congratulations! The Initial Review for your No More Than Minimal Risk human subjects research protocol TO-87-3564 entitled "Respiratory Health Effects of CS Riot Control Agent Exposure in Army Medical Department Basic Officer Leadership Course Trainees" was reviewed and approved for execution on July 02, 2015 by Dr. Edmund Howe, M.D., J.D., Chair IRB #1 under the provision of 32 CFR 219.110(b)(1)Suppl.F(7). This approval will be reported to the USU IRB #1 scheduled to meet on July 16, 2015.

The purpose of this study is to investigate self-reported acute respiratory health outcomes after exposure to CS riot control agent (tear gas) during the mandatory Mask Confidence Training (MCT) exercise conducted during Basic Office Leadership Course (BOLC). Individuals who agree to participate in this study will complete questionnaires approximately 24 hours prior to the MCT course and again at 24 hours and 14 days after the MCT course. Questionnaires will be correlated with CS exposure data (air sampling) obtained from the associated protocol TO-87-3516, entitled "Evaluation of Urinary Biomarker Assay of Exposure to O-Chlorobenzylidene Malononitrile during U.S. Army Mask Confidence Training Exercises." Up to 120 individuals are authorized to participate in this study.

You are reminded that local Command approval must be obtained prior to implementation of research activities.

Authorization to conduct protocol TO-87-3516 will automatically terminate on July 01, 2016. If you plan to continue data collection or analysis beyond this date, IRB approval for continuation is required. Please submit a USU Form 3204 A/B, application for continuing approval 60 days prior to your termination date. You will receive a reminder from IRBNet.

You are required to submit amendments to this protocol, changes to the informed consent document (if applicable), adverse event reports, and other information pertinent to human research for this project in IRBNet. No changes to this protocol may be implemented prior to IRB approval. If you have questions regarding this IRB action or questions of a more general nature concerning human participation in research, please contact Micah Stretch at 301-295-9534 or micah.stretch@usuhs.edu.

Edmund G. Howe, M.D., J.D.
Chair, IRB #1

Concur / Nonconcur

Arthur L. Kellerman, MD, MPH
Professor and Dean, School of Medicine

JUL - 2 2015
Date

This document has been signed electronically.

"Electronic Signature Notice: In accordance with the "Government Paperwork Elimination Act" (GPEA) (Pub.L. 105-277; codified at 44 USC 3504); Federal and DOD applicable instructions, directives and regulations, documents have been electronically signed and authorized by all who have been required to do so. These signatures have the same effect as their paper-based counterparts. Verification is retained within our protected electronic records and audit trails."

Learning to Care for Those in Harm's Way

APPENDIX D. INFORMATION SHEET AND CONSENT FORM

UNIFORMED SERVICES UNIVERSITY

BETHESDA, MARYLAND

This consent form is valid only if it contains the "USUHS IRB Approved" stamp. Do not sign this form or participate in this research if the IRB stamp is not present or if it has expired.

Consent for Voluntary Participation in a Research Study

1. INTRODUCTION OF THE STUDY

You are being asked to participate in concurrent research studies entitled, "Evaluation of Urinary Biomarker Assay for Exposure to O-chlorobenzylidene malononitrile (CS Riot Control Agent) during U.S Army Mask Confidence Training (MCT) Exercises" and "Self-Reported Respiratory Outcomes of CS Riot Control Agent Exposure in AMEDD Basic Officer Leadership Course Trainees" coordinated by the Uniformed Services University of the Health Sciences (USUHS), Bethesda, Maryland. Your participation is voluntary. Refusal to participate will not result in any punishment or loss of benefits to which you are otherwise permitted. Please read the information below, and ask questions about anything you do not understand, before deciding whether to take part in these studies.

2. PURPOSE

a. "Evaluation of Urinary Biomarker Assay for Exposure to o-chlorobenzylidene malononitrile (CS Riot Control Agent) during U.S Army Mask Confidence Training (MCT) Exercises" (Study A)

The purpose of this study is to investigate the relationship between exposure to CS riot control agent and the concentration of the metabolite 2-chlorohippuric acid (CHA) found in urine after exposure. A better understanding of the relationship between exposure and metabolite concentration would assist medical and law enforcement professionals to more effectively perform their duties in CS exposure cases.

b. "Self-Reported Respiratory Outcomes of CS Riot Control Agent Exposure in AMEDD Basic Officer Leadership Course Trainees" (Study B)

The objective of this research study is to document any relationship of CS exposure to specific acute respiratory symptoms in U.S. Army Officers enrolled in the Army Medical Department (AMEDD) Basic Officer Leadership Course (BOLC). The study will examine any potential association between CS exposure during MCT and new-onset acute respiratory outcomes post-exposure at two points in time (24 hours and 14 days). Previous studies have described an association between CS exposure (during MCT) and increased rate of acute respiratory illness and so results from this study could inform policy regarding BOLC training to reduce respiratory morbidity and lost duty days.

USUHS IRB APPROVED
Approved: 26 JULY 2016
Expires: 01 JULY 2016

3. PROCEDURES

Depending on which part of this research you agree to participate in, you will be asked to do different things.

If you agree to participate in the biomarker study (study A), you will be asked to provide urine samples (approximately 10-15ml or 2-3.5 teaspoons) the day of your regularly scheduled BOLC training in the morning before your MCT exercise and again at approximately 2, 8 and 24 hours after you complete the MCT exercise. Within 24 hours of collects, samples will be sent to the CDC for analysis. In addition, you will be fitted with a personal air-sampling pump during the MTC exercise. The pump will allow us to know how much CS vapor and particulates you have been exposed to and is a standard occupational exposure sampling method.

If you agree to participate in the respiratory outcome study (study B), you will be asked to complete a brief questionnaire prior to your MCT exercise and again at approximately 24 hours and 14 days after completing the MCT exercise. You will be asked to complete these questionnaires at the same time urine samples are collected for study A. The questionnaires ask about your basic demographic information, general respiratory health and symptoms you may have experienced after completing the MCT exercise. You may skip any questions that make you feel uncomfortable. To understand the relationship (if any) between your self-reported respiratory health/ symptoms and CS exposure, we will need to use the data collected from your personal air-sampling pump used in study A. **As a result, to participate in study B you must also participate in study A.**

Standard operating procedures, personal protective equipment, training tasks, and time in the CS chamber will not be altered in any way by either study.

4. POSSIBLE BENEFITS FROM BEING IN THIS STUDY

These projects are being conducted for research purposes only and are not intended to directly benefit you.

5. COMPENSATION

There is no financial compensation for your participation in this research.

6. POSSIBLE RISKS OR DISCOMFORTS FROM BEING IN THIS STUDY

There are no known expected risks or discomfort from being in either or both studies. You may skip any survey questions that make you feel uncomfortable.

7. RIGHT TO WITHDRAW

You may decide to stop taking part in either or both studies at any time. Your relations with both BOLC and USU faculty and staff will not be changed in any way if you decide to end your participation in the study.

8. RECOURSE IN THE EVENT OF INJURY

If at any time you believe you have suffered an adverse event as a result of participating in this research project, you should contact the Director of Human Research Protections Programs at the Uniformed Services University of the Health Sciences, Bethesda, Maryland 20814-4799 at (301) 295-9534. This office can review the matter with you, provide information about your rights as a subject, and may be able to identify resources available to you. If you believe the government or one of the government's employees (such as a military doctor) has injured you, a claim for damages (money) against the federal government (including the military) may be filed under the Federal Torts Claims Act. Information about judicial avenues of compensation is available from the University's General Counsel at (301) 295-3028.

9. PRIVACY AND CONFIDENTIALITY

All information you provide as part of this study will be confidential and will be protected to the fullest extent provided by law. Your surveys and urine samples will contain no personally identifiable information. Only the key linking your name to a unique study identifier and the consent form will contain your name. Both documents will be physically secured and held separate from the completed surveys and urine samples. The CDC will receive coded samples and will destroy any remaining samples once the analysis has been completed. Once the final round of surveys is complete and data are linked in the analysis data set, the masker key file will be destroyed. All records related to this study will be accessible to those persons directly involved in conducting this study and members of the USUHS Institutional Review Board (IRB), which provides oversight for protection of human research volunteers. In addition, other federal agencies that help protect people who are involved in research studies may need to see the information you give us. Other than those groups, records from this study will be kept confidential to the fullest extent of the law. Scientific reports that come out of this study will not use your name or identify you in any way, and all reporting of results from this study will be in the aggregate. As a military service member, please be advised that under Federal Law, your confidentiality cannot be strictly guaranteed.

USUHS IRB APPROVED
Expires: 01 JUL 2016

10. CONTACT FOR QUESTIONS OR PROBLEMS

If you have questions about this study, please contact either, LTJG Maccon A Buchanan (maccon.buchanan@usuhs.edu) or CPT Matthew Holuta (matthew.holuta@usuhs.edu) . If you have questions about your rights as a research subject, you should call the Director of Human Research Protections Program at USUHS at (301) 295-9534. The director is your representative and has no connection to the researcher conducting this study.

****IF YOU HAVE ANY QUESTIONS PLEASE FEEL FREE TO ASK THEM****

SIGNATURE OF RESEARCH PARTICIPANT OR LEGAL RESPRESENTATIVE
You have read (or someone has read to you) the information in this consent form. You have been given a chance to ask questions and all of your questions have been answered to your satisfaction.

BY SIGNING THIS CONSENT FORM, YOU FREELY AGREE TO TAKE PART IN THE RESEARCH IT DESCRIBES.

I consent to participate in the study (A): "Evaluation of Urinary Biomarker Assay for Exposure to O-chlorobenzylidene malononitrile (CS Riot Control Agent) during U.S Army Mask Confidence Training (MCT) Exercises"

Signature	Print Name	Date

I consent to participate in the study (B): "Self-Reported Respiratory Outcomes of CS Riot Control Agent Exposure in AMEDD Basic Officer Leadership Course Trainees"

Signature	**Print Name**	**Date**

SIGNATURE OF INVESTIGATOR

You have explained the research to the participant, or his/her legal representative, and answered all of his/her questions. You believe that the volunteer subject understands the information described in this document and freely consents to participate.

Investigator's Signature	Date (must be the same as the participant's)

Investigator's Printed Name

APPENDIX E. BOLC TRAINING SCHEDULE

13JUL

0530-0630	Movement to TTB	FSH
0600-0630	Arrived from Ft Sam/ Formation	TS 22
0600-0615	Sick Call Sign In	TS 22
0630-0730	Personal Hygiene/ Breakfast (and 2x MREs)	TS 22
0700-0800	Weapon Draw from TSC (Team 4 with detail)	TS 22
0730-0800	Cadre BUB	TS 22
0800-0900	Weapon Issue	TS 22
0830-0900	Cadre Prep for TC3 Class	TS 22
0900-1200	TC3 Med Tasks, Vehicle Load (by PLT)	TS 22
1200-1230	Lunch	TS 22
1230-1600	APFT Testing (M16, Medevac Request, M9)	TS 22
1230-1600	A Co	TS 22
	1230-1400: M9	TS 22
	1400-1500: M16	TS 22
	1500-1600: MEDEVAC Request	TS 22
	B Co	TS 22
	1230-1330: M16	TS 22
	1330-1430- MEDEVAC Request	TS 22
	1430-1600: M9	TS 22
1600-1630	Cadre TC3 Demo	TS 22
1700-1730	Student Leadership Meeting	TS 22
1700-1800	Dinner	TS 22
1800-1900	Student BUB	TS 22
1600-0600	Night OIC	TS 22

14JUL

0430-0800	Chow Detail	TS 22
0430-0630	Foot March (Record) Stagger SP Time - 0430, 0445	TS 22
0500-0515	Sick Call Sign In	TS 22
0630-0730	Breakfast/ Personal Hygiene	TS 22
0730-0800	Cadre BUB	TS 22
0800-0830	Movement to NBC Chamber (by Vehicle)	TS 22
0830-1600	NBC Chamber (1-2 PLT)	TS 22
0800-1600	Role I/ Convoy Ops/ Role III Tour (3-4 PLT)	TS 22
0800-1600	Land Nav Trng/ Role II (5-6 PLT)	TS 22
1630-1700	Student Leadership Meeting	TS 22
1700-1715	Chow Detail	TS 22
1730-1900	Dinner	TS 22
1930-2000	Student BUB	TS 22
1600-0600	Night OIC	TS 22

15JUL

0430-0800	Chow Detail	TS 22
0430-0630	Night Land Nav (A Co)	TS 22
0500-0515	Sick Call Sign In	TS 22
0530-0630	PRT (B Co)	TS 22
0630-0730	Breakfast	TS 22
0730-0800	Cadre BUB	TS 22
0800-0830	Movement to NBC Chamber (by Vehicle)	TS 22
0830-1600	NBC Chamber (3-4 PLT)	TS 22
0800-1600	Role I/ Convoy Ops/ Role III Tour (5-6 PLT)	TS 22
0800-1600	Land Nav Trng/ Role II (1-2 PLT)	TS 22
1600-1630	Student Leadership Speech with ROLE OICS	TS 22
1630-1700	Student Leadership Meeting	TS 22
1700-1715	Chow Detail	TS 22
1730-1900	Dinner	TS 22
1930-2000	Student BUB	TS 22
1600-0600	Night OIC	TS 22

16JUL

0430-0800	Chow Detail	TS 22
0430-0630	Night Land Nav (B Co)	TS 22
0500-0515	Sick Call Sign In	TS 22
0530-0630	PRT (A Co)	TS 22
0630-0800	Breakfast	TS 22
0730-0800	Cadre BUB	TS 22
0800-0830	Movement to NBC Chamber (by Vehicle)	TS 22
0830-1600	NBC Chamber (5-6 PLT)	TS 22
0800-1600	Role I/ Convoy Ops/ Role III Tour (1-2 PLT)	TS 22
0800-1600	Land Nav Trng/ Role II (3-4 PLT)	TS 22
1600-1700	Weapon Cleaning	TS 22
1600-1700	Lynch Leadership/ Citizen Soldier Board	TS 22
1630-1700	Student Leadership Meeting	TS 22
1700-1730	Chow Detail	TS 22
1700-1800	Weapon T/I	TS 22
1700-1800	Dinner	TS 22
1930-2000	Student BUB	TS 22
1600-0600	Night OIC	TS 22

17JUL

0400-0415	Sick Call Sign in	TS 22
0400-0415	Cadre BUB #1	TS 22
0415-0430	Student Formation/ Land Nav Brief	TS 22
0430-0930	Land Navigation Test	TA 6
0900-0915	Cadre BUB #2	TS 22
0915-0930	Cadre Prep for Demo	TS 22
0930-1030	Cadre Rehearsal Convoy Demonstration	TS 22
1030-1130	Cadre Convoy Demonstration	TS 22
1130-1230	Weapon T/I to TSC (Team 4 with detail)	TS 22
1130-1230	Lunch	TS 22
1130-1400	TTB Recovery	TSC / TS 22
1230-1300	Class Photo	TS 22
1345-1400	Student Formation	TS 22
1400-1430	Movement to Fort Sam Houston	TS 22

APPENDIX F. ASSOCIATION OF SELECT VARIABLES WITH CASE STATUS

Table 9. Characteristics of Participants Meeting Case Criteria

	Non-case (n= 70)		Case (n=4)		P Value*
	n	*%*	*n*	*%*	
History of asthma	3	4	1	25	0.20
History of allergies	12	17	2	50	0.16
Sick contacts prior to exposure					
Same Platoon	40	57	4	100	0.14
Shared Tent	36	51	4	100	0.12
Past Smoker	3	4	1	25	0.20
Gender					
Female	36	51	2	50	1.00
Male	34	49	2	50	
Physical Fitness Test					
< 180	15	21	2	50	
180-269	36	51	1	25	0.34
>269	19	27	1	25	
BMI					
Overweight(and Obese)	32	46	3	75	0.34
Obese	5	7	1	25	0.26
Absence from work in the past year	13	19	0	0	1.00
Prior exposure to CS	9	13	1	25	0.45
Chamber Date					
14-Jul-15	22	31	0	0	
15-Jul-15	30	43	2	50	0.56
16-Jul-15	22	31	2	50	
Training Company					
Alpha	33	47	0	0	0.12
Bravo	37	53	4	100	
Training Platoon					
1st	10	14	0	0	
2nd	11	16	0	0	
3rd	11	16	0	0	0.77
4th	17	24	2	50	
5th	8	11	1	25	
6th	13	19	1	25	

Branch of Service					
Dental Corps	5	7	1	25	0.69
Medical Corps	24	34	1	25	
Medical Service Corps	30	43	2	50	
Medical Specialist Corps	2	3	0	0	
Nurse Corps	2	3	0	0	
Veterinary Corps	7	10	0	0	

**Fisher's exact test*

Table 10. Exposure Related Attributes of Participants Meeting Case Criteria

	Non-case *(n= 70)*		**Case** *(n=4)*		**P Value***
	n	*%*	*n*	*%*	
More than one breath without respirator	35	47	3	75	0.62
Perceived discomfort during exposure					
Mild	17	23	2	50	0.34
Moderate	32	43	2	50	
Severe	21	28	0	0	
Acute effects duration >30 min.	7	9	0	0	1.00
Allergy Symptoms Present (at least moderate)					
Pre**	3	19	1	50	0.51
24hrs Post-exposure**	1	6	1	50	0.45
7 days Post-exposure**	1	6	2	100	0.03
NA	58	78	2	50	
Awakened from sleep by own coughing (7days post)	1	1	3	75	< 0.01
Physical Activity Degradation					
24hrs Post-exposure	2	3	0	0	1.00
7 days Post-exposure	2	3	2	50	0.01
Irritation Severity (moderate to severe symptoms)					
Shortness of Breath (24hrs)	1	1	1	25	0.11
Difficulty Breathing (24hrs)	1	1	1	25	0.11
Shortness of Breath (7 days)	0	0	1	25	0.05
Difficulty Breathing (7days)	0	0	1	25	0.05

**Fisher's exact test*

*** Those without the condition were excluded from the test*

Table 11. Exposure Related Attributes of Participants Meeting Case Criteria (continuous variables)

	Non-case *(n= 70)*		**Case** *(n=4)*		**P Value***
	mean	*sd*	*mean*	*sd*	
Time in Chamber *(minutes)*	05:31	01:26	05:55	00:29	0.57
CS Concentration *(mg/m3)**	2.68	0.99	3.90	0.65	0.03
Age	27	5.4	27	6.8	0.57
BMI	24.4	2.9	26.6	2.4	0.16
Time out of Mask *(seconds)*	00:09	00:02	00:08	00:01	0.95

* *t-test*

** *Independent-Samples Mann-Whitney U Test*

APPENDIX G. ASSOCIATION OF SELECT VARIABLES WITH EXPOSURE ABOVE 3.00 MG/MG^3

Table 12. Characteristics of Participants Among the 3.00 mg/m^3 Threshold Concentration Groups

Characteristic	< 3.00 mg/m^3 *(n= 40)*		≥ 3.00 mg/m^3 *(n=34)*		P Value*
	n	%	n	%	
History of asthma	2	5.0	2	5.9	1.00
History of allergies	7	17.5	7	20.6	0.77
Sick contacts prior to exposure					
Same Platoon	26	65.0	18	52.9	0.35
Shared Tent	24	60.0	16	47.1	0.35
Past Smoker	2	5.0	2	5.9	1.00
Gender					
Female	23	57.5	15	44.1	0.35
Male	17	42.5	19	55.9	
Physical Fitness Test					
< 180	8	20.0	9	26.5	
180-269	19	47.5	18	52.9	0.54
>269	13	31.0	7	20.6	
BMI					
Overweight(and Obese)	17	42.5	21	61.8	0.17
Obese	5	12.5	1	2.9	0.21
Absence from work in the past year	6	15.0	5	14.7	1.00
Prior exposure to CS	7	17.5	3	8.8	0.33
Chamber Date					
14-Jul-15	21	52.5	0	0.0	
15-Jul-15	15	37.5	15	44.1	< 0.01
16-Jul-15	4	10.0	19	55.9	
Training Company					
Alpha	25	62.5	8	23.5	< 0.01
Bravo	15	37.5	26	76.5	
Training Platoon					
1st	10	25.0	0	0.0	< 0.01
2nd	11	27.5	0	0.0	

3rd	4	10.0	7	20.6	
4th	11	27.5	8	23.5	
5th	1	2.5	8	23.5	
6th	3	7.5	11	32.4	
Branch Specialty					
Dental Corps	2	5.0	4	11.8	
Medical Corps	13	32.5	12	35.3	
Medical Service Corps	20	50.0	12	35.3	0.53
Medical Specialist Corps	0	0.0	2	5.9	
Nurse Corps	1	2.5	1	2.9	
Veterinary Corps	4	10.0	3	8.8	

**Fisher's exact test*

Table 13. Exposure Related Attributes of Participants Among the 3.00 mg/m^3 Threshold Concentration Groups

Characteristic	**< 3.00 mg/m^3** *(n= 40)*		**≥ 3.00 mg/m^3** *(n=34)*		**P Value***
	n	%	n	%	
More than one breath without respirator	22	55.0	16	47.1	0.64
Perceived discomfort during exposure					
Mild	12	30.0	7	20.6	
Moderate	18	45.0	16	47.1	0.60
Severe	10	25.0	11	32.4	
Acute effects duration >30 min.	3	7.5	4	11.8	0.70
Allergy Symptoms Present (at least moderate)					
Pre	1	2.5	3	8.8	0.56
24hrs Post-exposure	0	0.0	2	5.9	0.46
7 days Post-exposure	1	2.5	2	5.9	1.00
NA	34		28		
Awakened from sleep by own coughing (7days post)	1	2.5	3	8.8	0.33
Physical Activity Degradation					
24hrs Post-exposure	1	2.5	1	2.9	1.00
7 days Post-exposure	2	5.0	2	5.9	1.00

Irritation Severity (moderate to severe symptoms)					
Shortness of Breath (24hrs)	0	0.0	2	5.9	0.21
Difficulty Breathing (24hrs)	0	0.0	2	5.9	0.21
Shortness of Breath (7 days)	0	0.0	1	2.9	0.46
Difficulty Breathing (7days)	0	0.0	1	2.9	0.46
Nausea Present					
24hrs Post-exposure	0	0.0	6	17.6	0.01
7 days Post-exposure	2	5.0	1	2.9	1.00

**Fisher's exact test*

*** Those without the condition were excluded from the test*

Table 14. Exposure Related Attributes of Participants Among the 3.00 mg/m^3 Threshold Concentration Groups (continuous variables)

Characteristic	**< 3.00 mg/m^3** *(n= 40)*		**≥ 3.00 mg/m^3** *(n=34)*		**P Value**
	mean	*sd*	*mean*	*sd*	
Time in Chamber *(min.)*	05:30	01:33	05:35	01:12	0.98**
Time out of Mask *(sec.)*	00:08	00:03	00:09	00:02	0.11**
CS Concentration	1.97	0.62	3.66	0.47	< 0.01*
Age	27.05	5.9	26	4.7	0.22**
BMI	24.2	3.2	25.0	2.4	0.22*

**t-test of mean values*

*** Mann-Whitney Test*

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